THE MEDICAL JOURNAL OF AUSTRALIA

VOL. II.—36TH YEAR. SYDNEY, SATURDAY, OCTOBER 1, 1949. No. 14.

Table of Contents.

[The Whole of the Literary Matter in THE MEDICAL JOURNAL OF AUSTRALIA is Copyright.]

ORIGINAL ARTICLES— Page

Studies on the Epidemiology of the 1947-1948 Epidemic of Poliomyelitis in South Australia, by R. V. Southcott, M.B., B.S., D.T.M. and H., N. D. Crosby, M.B., B.S., and N. S. Stenhouse, B.Sc. 481

Impediments to Progress in Medical Education, by E. S. Meyers 496

Variants of the Rh Type: An Interesting Family Study of an Rh Gene Alleiomorphic to D, by Aileen M. Delaney, B.Sc. 500

Syphilis Resurgens, by E. H. Molesworth, M.D., F.R.A.C.P., Dip. Rad. 502

REPORTS OF CASES—

A Case of Asthma and Eosinophilia in an Ex-Prisoner of War, by W. B. Stafford, M.D. 505

REVIEWS—

A Year Book of Neurology, Psychiatry and Neuro-Surgery 507

Minor Surgery 507

Muscles, Testing and Function 507

The Szondi Test 508

Medicine 508

BOOKS RECEIVED 508

LEADING ARTICLES—

The Adreno-Cortical Hormone in Rheumatoid Arthritis 509

CURRENT COMMENT—

Nocturnal Secretion in Gastric Ulcer 510

Prophylactic Sulphanilamide Therapy in Rheumatic Fever 511

Normal Iron Reserves 511

ABSTRACTS FROM MEDICAL LITERATURE— Page

Medicine 512

SPECIAL ABSTRACT—

Drugs in the Treatment of Rheumatic Disorders 514

CORRESPONDENCE—

The Pain of Pleurodynia 516

Doctors and Marital Guidance 516

The Blind Deaf 516

The Royal Prince Alfred Hospital Cancer of the Uterus Follow-Up 516

Clinical Uses of Basal Body Temperature Graphs in Practice 516

OBITUARY—

Hibbert Alan Stephen Newton 517

Ivan Blaubaum 519

Robert Spencer Godsall 519

AUSTRALASIAN MEDICAL PUBLISHING COMPANY, LIMITED—

Annual Meeting 519

DISEASES NOTIFIED IN EACH STATE AND TERRITORY OF AUSTRALIA 519

AUSTRALIAN MEDICAL BOARD PROCEEDINGS—

New South Wales 520

NOMINATIONS AND ELECTIONS 520

NOTICE 520

MEDICAL APPOINTMENTS 520

DIARY FOR THE MONTH 520

MEDICAL APPOINTMENTS: IMPORTANT NOTICE .. 520

EDITORIAL NOTICES 520

STUDIES ON THE EPIDEMIOLOGY OF THE 1947-1948 EPIDEMIC OF POLIOMYELITIS IN SOUTH AUSTRALIA.

By R. V. SOUTHCOTT, M.B., B.S., D.T.M. and H.,
Faculty of Medicine, University of Adelaide,

AND

N. D. CROSBY, M.B., B.S.,
Faculty of Medicine, University of Adelaide,

WITH THE COLLABORATION OF

N. S. STENHOUSE, B.Sc.,
Section of Mathematical Statistics, Commonwealth Scientific and Industrial Research Organization.

IN South Australia in the summer of 1947-1948 an epidemic of poliomyelitis occurred. The notifications of this disease for the final four weeks of 1947 were successively 3, 3, 18 and 19, these making a total of 43 cases out of a total of 55 cases notified for 1947 for a population of 646,216 in South Australia. There was considerable public interest in, and alarm at, the rising incidence of the disease. It was feared that these rapidly rising figures might herald an epidemic of considerable proportions, such as had occurred in the summer of 1937-1938 in South Australia, as well as in the other States of the Australian Commonwealth.

Cases of the disease occurred in both urban and rural areas (Figures I and II). As many of these rural cases were from apparently isolated farms and settlements, it was realized that this was an excellent opportunity to study the vexed problem of the epidemiology of poliomyelitis, and particularly to investigate the mode of transmission of the disease. The staff of the Northfield Infectious Diseases Hospital, where the majority of the patients were isolated, had obtained no evidence of contact between any of these earlier paralytic patients.

For the investigation of the epidemic, the Crippled Children's Association of South Australia offered a grant which was accepted by the University of Adelaide. The South Australian Government offered further financial aid, which proved necessary. The Faculty of Medicine appointed us for this purpose, giving us wide scope as to the way in which the work was to be done. The field work was started in late December, 1947, and lasted until early February, 1948.

HISTORICAL INTRODUCTION.

Poliomyelitis appears to have arisen, or at least to have assumed significance, in comparatively recent historical times. The first cases generally accepted as of poliomyelitis were described by Badham in 1836. The first epidemic recorded for South Australia, of fourteen cases, occurred in 1895 at Port Lincoln, a seaport with a population of 1500 persons at the time. This appears also to be the first recorded Australian epidemic. Altmann (1897), in recording this epidemic, stated that there had been no previous case at Port Lincoln since 1887, when one case had occurred. This 1887 case is accepted by Berteniue (1947) as the first recorded Australian case of poliomyelitis. Altmann recorded a number of data for his fourteen cases, which leave no doubt as to the correctness of the diagnosis. However, he made no reference to concomitant non-paralytic[1] or "abortive" cases, nor to any other associated illnesses. Non-paralytic cases of poliomyelitis were first described by Caverley (1894, 1896, 1914) for an epidemic at Rutland, in Vermont, United States of America; but the existence of these non-paralytic cases was not widely known or accepted until the publication

[1] In this article we use the terms "non-paralytic" and "abortive" interchangeably, but prefer the former term.

of Wickman's (1905, 1913) classic studies of the disease in Sweden.

In the following years, epidemics were recorded for other Australian States: for New South Wales in 1904 (Blackall, 1904; Litchfield, 1904; Wade, 1904); for Queensland in 1904, 108 cases (Ham, 1905); for Victoria in 1908, 135 cases (Stephens, 1908). The increasing size of these epidemics is of interest. After the early epidemic recorded above, there is no evidence of any further epidemic in South Australia until the summer of 1921-1922. On February 22, 1922, poliomyelitis became a notifiable disease in this State, following the occurrence of six cases in neighbouring streets at Semaphore, a seaside suburb of Adelaide (Central Board of Health, Adelaide, 1922). There were 47 cases of poliomyelitis notified in 1922, 42 of which occurred in the first half of 1922. As the discussion on the seasonal incidence will indicate later, this shows that there was an epidemic of poliomyelitis in that summer; furthermore, we have some data of cases occurring in December, 1921.

The Technique and Scope of the Present Investigation.

A preliminary survey of the notifications suggested that, as our time and facilities were limited, the best results would come from a detailed investigation of the extra-metropolitan[1] cases, for two main reasons: (i) the numbers of contacts of these cases and the dispersal of these contacts would be limited, which would ease the task of attempting to trace contacts; (ii) the relationship of the disease to hygiene, if any such existed, would stand out more in rural communities, because in urban communities the deep drainage system of sewerage eliminates most of the enteric diseases.

These suppositions were not entirely borne out. For example, the families concerned in the poliomyelitis at Clarendon and Noarlunga, these being small rural towns 18 and 21 miles respectively from Adelaide, had members who daily proceeded by road to Adelaide for employment. Furthermore, it may be stated that "rural isolation" scarcely exists any longer, this being due to the transport facilities of modern times—rail, road and air. Thus, what appeared on a number of occasions from first reports to be an isolated case, always proved after detailed examination to be involved in a network of human contact ranging over considerable distances. We found no occurrence of the disease in families or individuals living in complete isolation.

While we had decided to focus the investigations in the field on the rural cases, we did not wish to lose any data that we could possibly obtain. We therefore sent out the following preliminary *questionnaire* sheet, with an accompanying letter. This was first sent out on January 7 to all the "notified" patients.

Information Required.

Last day of attendance at school (hour and date).
Name and locality of school.
Last attendance at Church or Sunday School.
Locality of Church or Sunday School.
The first day that the illness was noticed.
The first day that the patient was attended by a doctor.
Name and address of doctor.
Symptoms of illness occurring in the last ten days:

	Date		Date
Headache		Vomiting	
Fever		Diarrhœa	
Stiff neck		Lassitude	
Cold		Catarrh	

Any special trips made by the family or patient in the last 18 days prior to illness.

Any visitors from a distance in the last 18 days prior to illness.

Could you collect samples of the flies about the house and outside, and keep them until we collect them?

[1] We use the terms "metropolitan" and "extrametropolitan" largely in place of the terms "urban" and "rural", since many of the larger communities in the country are as "urbanized" as the inhabitants of the outer parts of Adelaide. In most cases the terms are used synonomously; but where precision is required in the text then the former are used. The dividing line is taken as a circle of radius ten miles, centred on Adelaide.

Simultaneously we began field investigations with rural cases near Adelaide. For this we had "roneoed" a pair of "extraction sheets" for our own use, on which were to be logged all the data obtained in the survey, covering many items. However, we soon saw that we should not have time to interview all the urban and rural patients to make these inquiries. We wished to obtain similar data for the urban and rural series, for mutual controls. Furthermore, we saw that many of the data that we required could be obtained as accurately by postal *questionnaire* as by personal interview. Accordingly we expanded the *questionnaire* to four "roneoed" pages, which are reproduced below.

HIGHLY CONFIDENTIAL

Number.....
Surname..... Christian names.....
Age..... Date of birth..... Sex..... Height.....
Location of residence at the onset.....
How long resident there..... Occupation of patient.....
Name of head of household..... Occupation.....
Occupational address of head of household.....
To whom should further communications be sent?.....
Relation of patient to head of household.....
What other members of family live in household. Give names and ages.

Surname	Christian names	Age	Occupation and occupational address. If school, state school and grade.
.....	.....	....	.....
.....	.....	....	.....
.....	.....	....	.....
.....	.....	....	.....
.....	.....	....	.....
.....	.....	....	.....

What other people live in the same household. Give same information.

.....	.....	....	.....
.....	.....	....	.....
.....	.....	....	.....

What Dr. was first called in to see patient?..... Date.....
State address of Dr. .....
What was the first hospital to which patient was sent? .....
Date.....

DETAILS OF ILLNESS

What were the first symptoms noted? State and give dates. (See following questions.)
Were the following symptoms present? State yes or no, giving dates.

Symptom	Yes/No	From (date)	to (date)
Headache	.....	.....	.....
Feverishness	.....	.....	.....
Sore throat	.....	.....	.....
Stiff neck	.....	.....	.....
Desire to vomit	.....	.....	.....
Vomiting	.....	.....	.....
Cough	.....	.....	.....
Back pains	.....	.....	.....
Diarrhœa	.....	.....	.....
Tired feeling	.....	.....	.....
Stomach pains	.....	.....	.....
Paralysis	.....	.....	.....

CONTACTS

Was there any contact with another patient suffering from infantile paralysis in this epidemic? If so, state details.
.....
.....
Was there any contact between the patient and a case of infantile paralysis in previous epidemics? If so, give details.
.....
.....

LOCAL ILLNESSES

What illnesses were occurring in your neighbourhood at the time of onset of the disease? Particularly would you note coughs, sore throats, bilious attacks, diarrhœa, vomiting. Give also the dates these ailments occurred.
.....
.....
.....
.....
Were members of the family affected in these outbreaks? If so, give details.....
.....
Did a doctor see these patients?..... If so, state which doctor.....

What domestic animals and birds do you keep, stating how many of each, and state if any illnesses, particularly if any animal or bird appeared paralysed.....
.....
.....

What visits were made away from home in the 30 days prior to the onset of the illness.....
.....
.....

Mode of travel.....
What visitors from a distance over the last 30 days.....
.....

Any recent dental extractions.....
Have the patient's tonsils been removed.....
State when and where tonsils removed .....
.....

Was school attended within 30 days?.....
State last date school attended.....
State the school concerned.....
Sunday School.....
Church .....
Picnics, parties, dances, etc., attended within 30 days.....
.....

Food suppliers

Milk—what dairy..... Scalded or not.....
Butter—where bought..... State what brand.....
Is cream consumed.....
Ice cream, sources and makes.....
Meat supplier..... Address.....
Vegetables.....

Water supply

.....
.....

Sanitation

Type—flush, pan or pit.....
Is the house well screened against flies.....
Are flies prevalent in the house.....
Are there rats or mice.....
Fleas, bedbugs, cockroaches, etc.....

The second postal *questionnaire* was made the basis of the personal investigations in the field, being either filled in on the spot, or, if it had already been returned by post, gone through again with the family, discussed, and if necessary corrected point by point.

After a trial investigation of a few cases in and around Adelaide, we investigated four rural areas together, when we were satisfied that our technique was sufficiently uniform. We then continued separately for the remainder of the field work.

The following was our general procedure of personal investigation in an individual rural case.

1. Interview the patient in hospital. At times this was not possible, owing to prior death, to respiratory or palatal paralysis *et cetera*. We were given access to the clinical notes of the hospitals.

2. Interview the doctor who attended the patient, to discuss the clinical features, and to inquire into what diseases were occurring locally.

3. Interview the family and close contacts. The second *questionnaire* was filled in with the family. A graphical diary was constructed on the spot in the later part of the investigation.

4. Interview any other person able to give useful information, particularly in the accurate dating of significant events.

There were many difficulties in the investigation. We were late in following the earlier cases. The different procedures for obtaining information furnished usually several sets of data for each individual case of poliomyelitis. Even in recent cases there would often be discrepancies between the first and second posted *questionnaires*, between these and information given personally by the patient, and again between that given by parents and relatives. These discrepancies occurred, not so much with the easily obtainable factual data, such as age, occupation *et cetera*, but more with the dates of human contacts, and the dates on which the various symptoms first occurred. We found the decision as to the date on which some perhaps significant contact occurred a recurring and difficult problem. In the whole of the investigation we found only two people who volunteered information from a diary.

In order to get our data as accurate as possible, we obtained as many versions as possible of facts and events that might have had some significance. Most people cooperated willingly. We could find no evidence that anyone deliberately misled us, but on more than one occasion erroneous information about contacts sent us on a long wild-goose chase.

In the field we refrained from asking leading questions for as long as possible. We asked a number of witnesses the same questions without informing them that we already had an answer. When different witnesses gave conflicting stories, as was often the case, if possible we confronted them with each other and let them decide mutually, and usually they reached agreement. If, on the final analysis of the written records some months afterwards, there were still discrepancies in the stories, we were sometimes able to discriminate satisfactorily between the stories of the different witnesses, deciding that some witnesses were more reliable than others, or that the bulk of the evidence was in favour of one of the versions. Our task in the field was aided in many cases by our already having some data on significant events—the date of admission of the patient to hospital, the date of onset of the disease *et cetera*—from the hospital records and the interrogation of the patient.

In each case, the field notes were converted to a typescript narrative by dictation to a stenographer. This was done as soon as possible after each field trip, usually one to three days after. Finally the events from the narrative were extracted and logged in time order, and converted to a diary for each area. With our increasing experience in the latter part of the investigation we diarized much of the data immediately in the field. Usually the diary would extend from a month before the onset of the poliomyelitis symptoms to some weeks afterwards, this latter depending on how long it was before we investigated that outbreak. We found it better to investigate the families personally some weeks after the occurrence of the disease rather than to do so immediately, as sometimes further transmission to other members of the family occurred, and these subsequent cases would be missed by too early an investigation. Two examples of the constructed diaries are shown later in the text (Figures VI and VIII). Once the diaries were constructed, discrepancies were easily observed.

In some cases in which the importance of the subject appeared to warrant it, further trips into the field were made to check points that had become important only after a study of the constructed diary. These trips were made from some weeks to some months after the original investigation. The furthest of these trips was to Swan Reach, some 76 miles from Adelaide by road. We found, however, that there was a limit to the value of these delayed investigations, as by then most of the detail had been forgotten. In some instances our efforts failed to fix important dates.

When paralytic poliomyelitis occurred in rural areas, we always found other illnesses of a minor nature. Frequently some of these minor illnesses were in the family of the sufferer. We might reasonably expect to find minor illnesses occurring in any community at any time, whether cases of poliomyelitis are present or not. However, we were struck by the resemblance borne by the symptoms in many of these cases of minor illness to the symptoms of paralytic poliomyelitis.

Many of the illnesses in which we came to take so great an interest were considered by the families to be too trivial for medical attention to be sought. Many of these trivial illnesses in children were sufficient to cause the child to be absent from school, and these absences were recorded in the half-day school attendance rolls. The school roll-book frequently came in the course of our investigation to serve as a diary for the dating of events in the families concerned in poliomyelitis. The cooperation of the school teachers in this aided us greatly. Furthermore, the school teachers were usually attentive observers of the children, and generally knew if the reason for a child's absence from school was medical or otherwise. However, if the illness had occurred on a Saturday or a Sunday, then there would be no record of any absence from school, unless the illness lasted beyond the week-end.

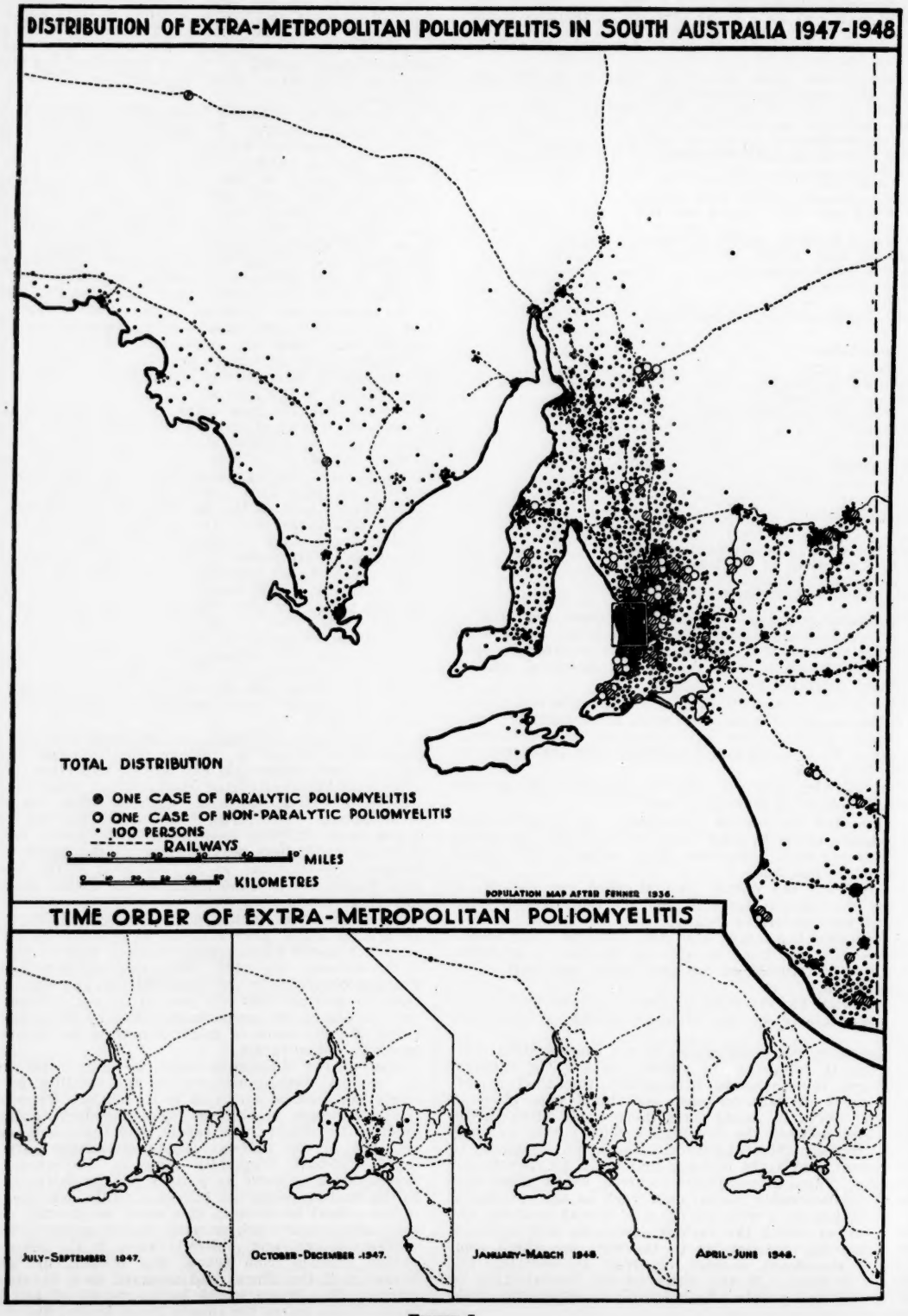
DISTRIBUTION OF EXTRA-METROPOLITAN POLIOMYELITIS IN SOUTH AUSTRALIA 1947-1948
TOTAL DISTRIBUTION
ONE CASE OF PARALYTIC POLIOMYELITIS
ONE CASE OF NON-PARALYTIC POLIOMYELITIS
100 PERSONS
RAILWAYS
MILES
KILOMETRES
POPULATION MAP AFTER FENNER 1936.
TIME ORDER OF EXTRA-METROPOLITAN POLIOMYELITIS
JULY-SEPTEMBER 1947.
OCTOBER-DECEMBER 1947.
JANUARY-MARCH 1948.
APRIL-JUNE 1948.

Figure I.

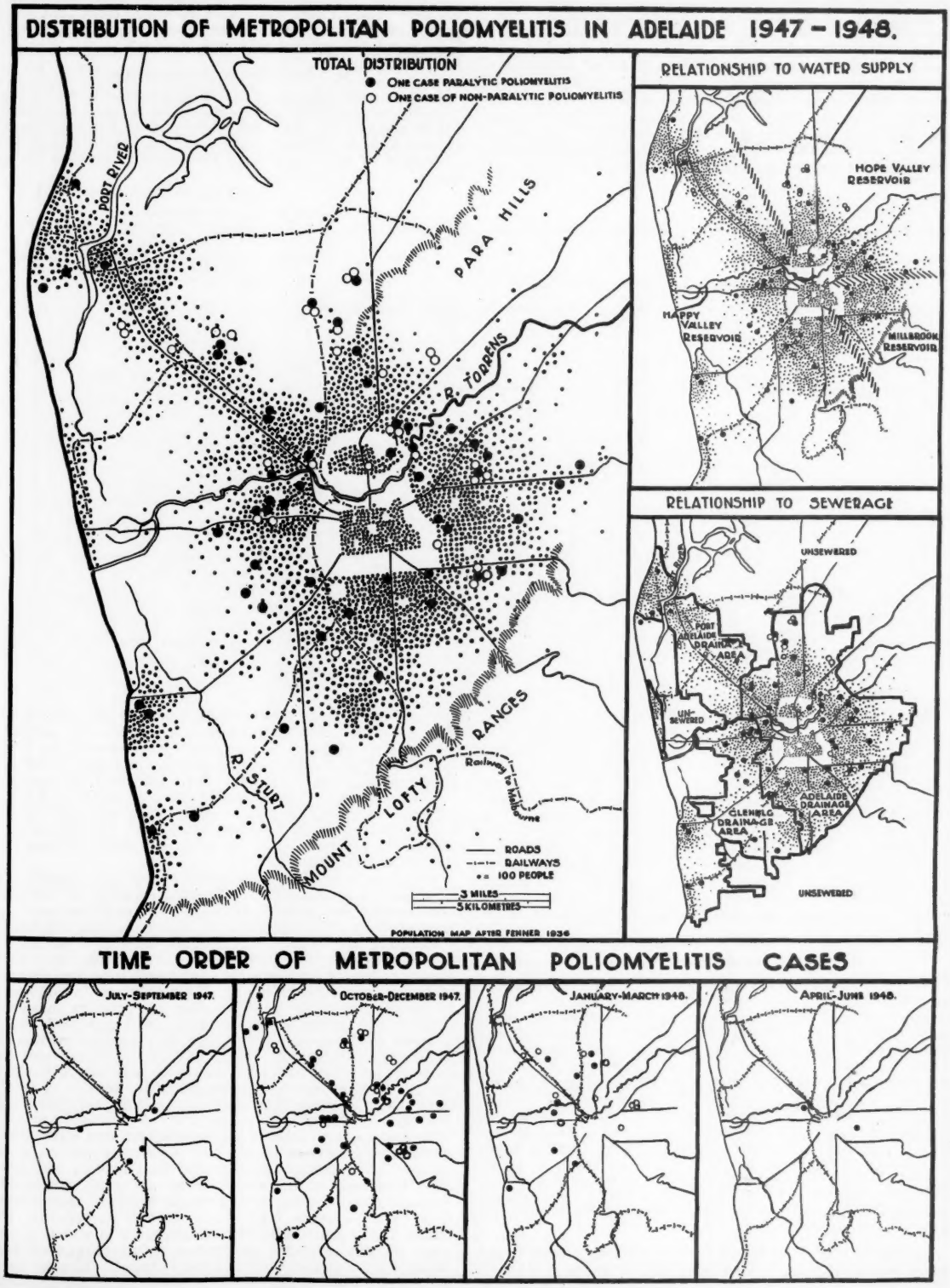
DISTRIBUTION OF METROPOLITAN POLIOMYELITIS IN ADELAIDE 1947 – 1948.
TOTAL DISTRIBUTION
ONE CASE PARALYTIC POLIOMYELITIS
ONE CASE OF NON-PARALYTIC POLIOMYELITIS
PORT RIVER
PARA HILLS
R. TORRENS
R. STURT
MOUNT LOFTY RANGES
Railway to Melbourne
ROADS
RAILWAYS
100 PEOPLE
3 MILES
5 KILOMETRES
POPULATION MAP AFTER FENNER 1936
RELATIONSHIP TO WATER SUPPLY
HOPE VALLEY RESERVOIR
HAPPY VALLEY RESERVOIR
MILLBROOK RESERVOIR
RELATIONSHIP TO SEWERAGE
UNSEWERED
PORT ADELAIDE DRAINAGE AREA
UNSEWERED
ADELAIDE DRAINAGE AREA
GLENELG DRAINAGE AREA
UNSEWERED
TIME ORDER OF METROPOLITAN POLIOMYELITIS CASES
JULY-SEPTEMBER 1947.
OCTOBER-DECEMBER 1947.
JANUARY-MARCH 1948.
APRIL-JUNE 1948.

FIGURE II.

The numbers of these cases of associated illnesses that we discovered in each rural community depended on various circumstances which determined the total number of people investigated. There was a small number of areas in which we investigated every case of illness of which we heard. The assigning of these minor illnesses to their correct relationship to poliomyelitis was a major problem.

The numbers of cases of illness investigated in each country area, and the numbers of paralytic and accepted non-paralytic cases of poliomyelitis found, are given in Table I.

Table I.

Results of Investigations in Rural Areas from which Poliomyelitis had been Reported.

Rural Area.	Population.	Number of Cases of Illness Investigated.	Number of Cases of Paralytic Poliomyelitis.	Number of Cases of Non-Paralytic Poliomyelitis.
Clarendon ..	441	47	3	7
Mount Gambier	7800[1]	29	2	5
Robe	448	18	2	1
Maitland	1200[1]	15	2	0
Angaston (1404) Nuriootpa (1209) Keyneton (299)	2912	14	4	4
Uraidla	425	14	2	3
Ardrossan ..	815	13	1	0
Clare and Black Springs	1950	12	1	2
Kadina	3200[1]	11	1	1
Jamestown ..	2050[1]	11	2	3
Swan Reach ..	463	8	2	2
Birdwood	602	4	1	3
Bordertown ..	1230	4	1	1
Noarlunga ..	307	4	1	3
Yankalilla	338	5	3	2
Gawler	4800[1]	3	1	0
Keith	366	3	1	1
Dublin	213	3	1	2
Salisbury ..	2350[1]	2	1	0
		220	32	40

[1] 1947 census. Other figures for population, 1933 census.

Of the first 34 extrametropolitan cases that occurred, we investigated personally 28, as well as a limited number of metropolitan cases. After early February, for private reasons, we were not able to continue with the field work, except for the Mount Gambier series which occurred in April, 1948. However, we continued to send out to all "notified" patients the second postal circular *questionnaire* until June, when the series was closed to bring the data into order for final analysis. The last patient of our series had the date of onset of his disease on June 2, 1948. There were 48 rural paralytic cases in all, of which 32 were investigated.

The Course of the Epidemic.

We have accepted the epidemic as lasting from July, 1947, until June, 1948, a period of twelve months. Prior to the first case admitted to our series no case had been notified for thirteen weeks, and after this first case there was a further seven weeks before another case was notified. After the last case admitted to our series there was a period of ten weeks for which no further case of poliomyelitis was notified. The number of cases occurring is shown in Figure III. In that figure the cases are logged by their date of onset for comparison with logging by the date of notification. Notification inevitably implies some delay; this depends on the interest being taken in poliomyelitis, which interest increases in the presence of an epidemic. The delay is due to the time taken for diagnosis and administration, and is well shown in the lower part of Figure III and Table II.

It will be seen that the 1947-1948 epidemic followed the usual seasonal pattern of epidemic poliomyelitis, indicated in Figure IV, which shows poliomyelitis notifications in South Australia from 1922 to 1948.

Of the five unnotified cases in the series of 103 paralytics, two were fatal. There were other paralytic cases that were notified only after a considerable delay. The great majority of the cases not notified were non-paralytic.

The Diagnosis of Poliomyelitis.

In South Australia all cases of poliomyelitis, both paralytic and non-paralytic, are notifiable, as is usual elsewhere. But in practice the diagnosis of other than frank paralytic poliomyelitis is attended with much uncertainty, and the proportion of the true sum of these that is notified varies widely.

Table IIa.

Data on the Present Epidemic.

Group.	Paralytic.	Non-Paralytic.	Notified.	Not Notified.
Urban	55	30	—	—
Rural	48	30	—	—
Total	103	60	126 (77·3%)	37
Grand total ..	163		163	

Table IIb.

Data on the Present Epidemic.

Period.	Notified.	Our Series.
July to December, 1947	51	107
January to June, 1948	75	56
Total ..	126	163

When once the existence of an epidemic of poliomyelitis was accepted, then the diagnostic criteria of paralytic poliomyelitis became more uniform, because the great majority of patients were admitted to Northfield Infectious Diseases Hospital. All the Northfield cases of paralytic poliomyelitis have been logged in our series. Not all subjects of paralytic poliomyelitis were admitted to the Northfield Infectious Diseases Hospital. Our series comprises 103 paralytic cases, of which 55 were metropolitan and 48 extrametropolitan.

Frank poliomyelitis is classified for our purposes as follows: (i) Encephalitic, indicating cerebral or mid-brain involvement as shown by any of the following: (*a*) irrationality, (*b*) diplopia, (*c*) coma in the absence of respiratory paralysis. (ii) Bulbar, as shown by any of the following: (*a*) difficulty in swallowing, (*b*) nasal regurgitation of food or fluid, (*c*) nasal tone and slurring of speech, not encephalitic in origin, (*d*) pooling of mucus in the oro-pharynx or naso-pharynx, (*e*) primary vasomotor collapse, (*f*) respiratory paralysis, not considered due to a spinal cord lesion. (iii) Spinal, as shown by evidence of paralysis of a group or groups of muscles, conceivably due to a spinal cord lesion. Usually it was not difficult to decide whether there was encephalitic, bulbar or spinal involvement, or whether one, two or three of these were present.

The diagnoses were made on clinical and pathological grounds (examination of the cerebro-spinal fluid for cellular and protein content, and post-mortem evidence). The likelihood of inclusion of other forms of encephalitis or meningitis *et cetera* is very small. Early in the epidemic there were several fatal cases of the encephalitic and bulbar type among children, the diagnosis of which became clear as the epidemic progressed. Our task was made easier by the virtual lack of other epidemic disease. There were a few cases of mumps (not now a notifiable disease in South Australia) with its mild encephalitis and myelitis,

and a few cases of diphtheria and measles (notifiable) during the epidemic.

We obtained as accurately as possible the data relating to the incidence and duration of the prodromal symptoms in the paralytic cases. The data were submitted to statistical analysis. Our collaborator (N.S.S.) found that the data of the duration of the symptoms were not sufficiently homogeneous for reliable estimates to be made. However, the data on the incidence of the symptoms were complete enough and gave results of value. We used these results as controls in the analysis of the symptoms in presumed non-paralytic poliomyelitis.

The incidence of the various prodromal symptoms in the paralytic cases—headache, stiff neck, fever, vomiting, nausea *et cetera*—will be given in the next section, where it will be shown that the incidence of symptoms in paralytic poliomyelitis and in non-paralytic poliomyelitis has a highly significant correlation.

Non-Paralytic Poliomyelitis.

As the investigation proceeded we became more and more impressed with the number of cases of minor sickness occurring in association with paralytic poliomyelitis, in which some or all of the following symptoms were present: headache, stiff neck, nausea, vomiting, fever, and sometimes transient muscular weakness not progressing to frank paralysis. When the investigation was completed, we had a large number of these cases, and we selected from them a number (60), both urban and rural, and submitted them to a statistical analysis of the incidence of the various symptoms and other features for a comparison with the same features of our series of paralytic poliomyelitis. Our selection of these cases of non-paralytic poliomyelitis for analysis depended on both the array of symptoms and the association with frank paralytic poliomyelitis cases. Some of the non-paralytic cases resembled the severest paralytic cases in these symptoms. Reference to Table I will show that in some rural areas there were many cases of minor illness.

The epidemic had the usual maximal summer incidence. As was expected, our investigations revealed a few outbreaks of "summer gastro-enteritis". Such outbreaks were found at Robe, Swan Reach and Maitland. Initially we thought that these outbreaks of diarrhœa might have some relation to poliomyelitis. However, as the investigation proceeded, we discovered various outbreaks of diarrhœa with no apparent relationship to the poliomyelitis cases. We came finally to the conclusion that these rural out-

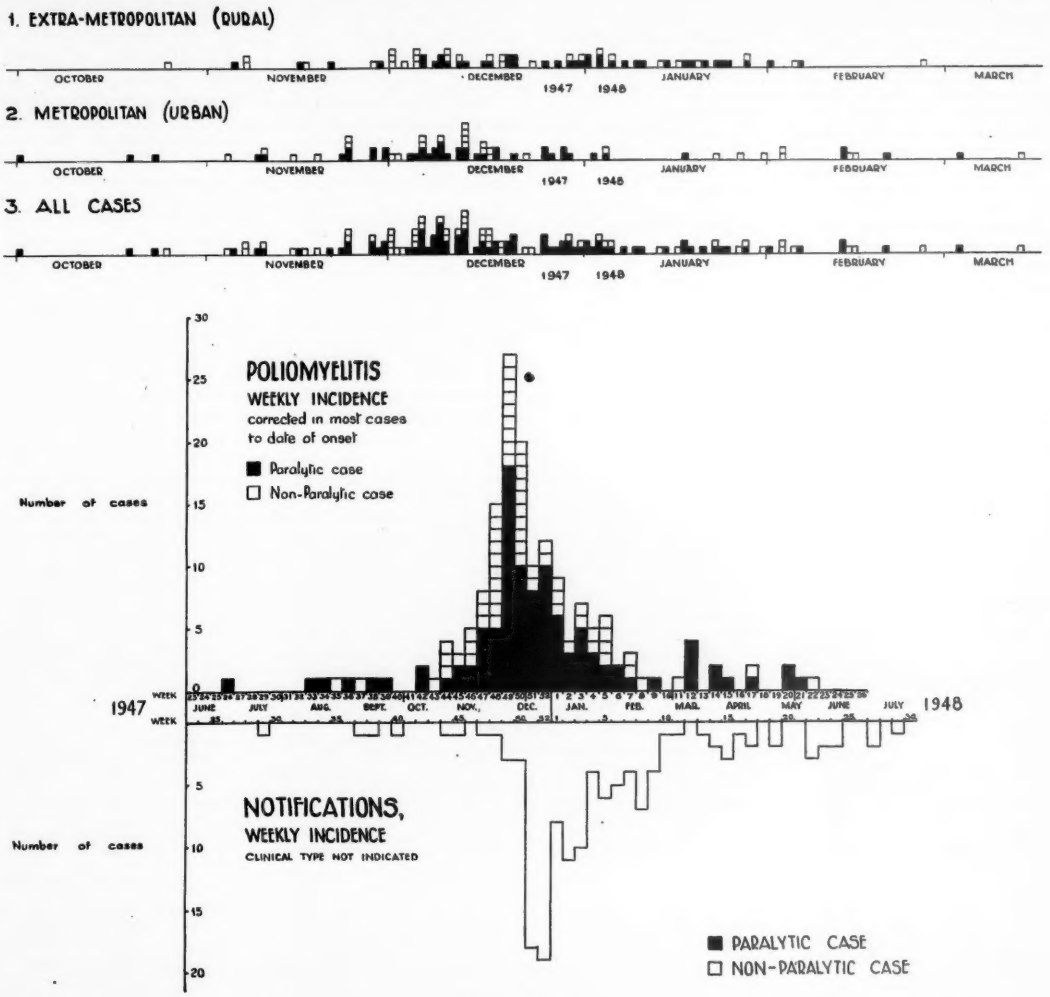

FIGURE III.

Incidence of poliomyelitis in South Australia, 1947-1948. Daily incidence, logged by date of onset.

UNIVERSITY OF MICHIGAN LIBRARIES

breaks of diarrhœa, which are in any case a normal feature of the summer, were not epidemiologically related to the poliomyelitis. We were strengthened in this belief by the low incidence of diarrhœa (6·4%) as a symptom of the paralytic cases in our series. Admittedly Theiler (1937) and Theiler and Gard (1940) have described a disease in mice in which both neural complications and diarrhœa occur; but as far as we can see there was no evidence that the diarrhœa outbreaks were related to the poliomyelitis.

The outbreak at Mount Gambier occurred in autumn, and it appears that the group of sicknesses there included sore throats and coryza, which begin to occur commonly at this time.

In some areas minor illnesses presented a variety of symptom patterns, which suggested that several different infections were coexistent in the community. In some paralytic cases there was evidence of a dual infection over a short period of time; in such cases we had no doubt that one illness was due to poliomyelitis virus, but we had reason to believe that certain symptoms had come from another infection. Such decisions about non-paralytic poliomyelitis complicated with a different infection were much more difficult. We deliberately omitted such complicated cases of non-paralytic poliomyelitis from our symptom analysis, and also cases from areas of probable mixed infections.

Table III compares the incidences of the symptoms in our series of paralytic and presumed non-paralytic cases.

The Analysis of the Symptom Incidence.

Our collaborator (N.S.S.) was presented with data of a series of 103 paralytic cases (55 urban, 48 rural) and a series of 60 presumed non-paralytic cases (30 urban, 30 rural). The nature of the data and the size of the series precluded the breaking down of the series into too many subdivisions for analysis. The data of the following subseries were compared: (i) urban paralytic against rural paralytic; (ii) urban non-paralytic against rural non-paralytic; (iii) first half of total paralytics against second half—that is, first 51 against last 51, the middle case being omitted; (iv) total paralytic against total non-paralytic. Various other types of analysis were attempted, but those listed above were the most important.

Results of the Analysis of the Symptom Incidence.—There are no mathematical grounds for making the following assumptions: (i) that the symptoms manifest in the first half of the paralytic series differ from those of the second half; (ii) that the symptoms of the urban paralytic series differ from those of the rural paralytic series; (iii) that the symptoms of the rural non-paralytic series differ from those of the urban non-paralytic series (the exception, "sore throat", is significant at the 5% level only, and in a large number of data such as this an occasional irregularity is to be expected); (iv) that the symptoms of the non-paralytic series differ significantly from the symptoms of the paralytic series. In the comparison of the paralytic and non-paralytic series the symptom "fever" occurs in a higher proportion of cases in the paralytic series than in the non-paralytic series. The difference is highly significant ($P = 0.0067$) and requires explanation (see later).

It must be borne in mind that the proportions given are in most cases only estimates. For example, of the 103 paralytics considered, 50 had the symptom "nausea", 21 did not have the symptom "nausea", and 32 were not known either to have or not to have the symptom "nausea". When the proportion $\frac{50}{50+21} = 70{\cdot}4\%$ is considered, the reservation must be made that the 32 cases not included may have greatly altered this figure. The true proportion may have been anywhere between 49% and 80%.

Comment.—In view of the method of selection of the cases, it was to be expected that some of the incidences would agree fairly closely. To us the most remarkable feature is that the correlation between the symptom incidences is so close and that we have been able to find a total of sixty cases that stood up to a rigorous comparison.

There are only two symptom incidences that differ significantly. The first incidence, that of "sore throat", which differed between urban non-paralytic and rural non-paralytic series, was not highly significant and was commented on earlier. The second discrepancy, fever incidence, between paralytics and non-paralytics, showed a highly significant difference. The discrepancy can be at least partly explained thus: nearly all the paralysed patients were admitted to hospitals where the temperatures were recorded as a routine measure, while the non-paralysed patients were rarely admitted to hospital. Hence the temperatures of the non-paralysed patients were seldom taken, and therefore fever would be recorded as a symptom

TABLE III.

Analysis of the Clinical Type and Symptom Incidence of Paralytic and Non-Paralytic Poliomyelitis.[1]

Series.	Clinical Types.			Incidence of Symptoms.											Fatal Outcome.
	Encephalitic.	Bulbar.	Spinal.	Headache.	Fever.	Sore Throat.	Stiff Neck.	Cough.	Back Pain.	Lassitude.	Nausea.	Vomiting.	Abdominal Pain.	Diarrhœa.	
Paralytic, first half	21·6 11/51	43·1 22/51	92·2 47/51	84·2 32/38	97·9 47/48	33·3 12/36	80·0 36/45	16·1 5/31	71·8 28/39	97·5 39/40	73·3 22/30	61·0 25/41	46·4 13/28	5·3 2/38	21·6 11/51
Paralytic, second half	19·6 10/51	35·3 18/51	90·2 46/51	86·4 38/44	100·0 47/47	41·7 15/36	83·0 39/47	15·2 5/33	79·5 35/44	90·5 38/42	70·0 28/40	63·0 29/46	27·3 9/33	7·5 3/40	17·6 9/51
Paralytic, urban ..	20·0 11/55	38·2 21/55	90·9 50/55	83·3 35/42	100·0 53/53	42·5 17/40	82·0 41/50	22·2 8/36	72·7 32/44	95·7 45/47	77·8 28/36	63·8 30/47	40·6 13/32	9·1 4/44	21·8 12/55
Paralytic, rural ..	20·8 10/48	39·6 19/48	91·7 44/48	87·5 35/40	97·7 42/43	33·3 11/33	81·4 35/43	7·1 2/28	80·0 32/40	91·4 32/35	62·9 22/35	58·5 24/41	31·0 9/29	2·9 1/34	16·7 8/48
Total paralytic	20·4 21/103	38·8 40/103	91·3 94/103	85·5 71/83	99·0 95/96	38·4 28/73	81·7 76/93	15·6 10/64	76·2 64/84	93·9 77/82	70·4 50/71	61·4 54/88	36·1 22/61	6·4 5/78	19·4 20/103
Non-paralytic, urban	— —	— —	— —	95·7 22/23	90·5 19/21	66·7 12/18	82·4 14/17	15·4 2/13	68·8 11/16	100·0 20/20	77·8 14/18	60·0 15/25	30·8 4/13	0·0 0/15	— —
Non-paralytic, rural	— —	— —	— —	73·7 14/19	81·3 13/16	33·3 6/18	63·2 12/19	16·7 2/12	57·1 8/14	78·6 11/14	78·6 11/14	71·4 15/21	33·3 3/9	12·5 2/16	— —
Total non-paralytic	— —	— —	— —	85·7 36/42	86·5 32/37	50·0 18/36	72·2 26/36	16·0 4/25	63·3 19/30	91·2 31/34	78·1 25/32	65·2 30/46	31·8 7/22	6·5 2/31	— —
Grand total, paralytic and non-paralytic	— —	— —	— —	85·5 106/124	95·5 126/132	41·7 45/108	78·9 101/128	15·7 14/89	72·6 82/113	93·1 108/116	73·5 75/102	63·2 84/133	34·9 29/83	6·4 7/109	— —

[1] The upper figure in each square is the percentage incidence. The lower figures are the absolute proportions from which the percentage was calculated. Thus in the top left-hand square there were 11 encephalitic cases out of 51, representing 21·6%.

only when pronounced. It is not known whether this explanation accounts for all the difference.

The results indicate that these sixty cases represent what must be very close to a pure array. We consider therefore that the results of the analysis establish the validity of the method of selection and the existence of non-paralytic poliomyelitis in this epidemic.

During our investigation in the field, we had no laboratory facilities as aids to diagnosis—for example, examination of the cerebro-spinal fluid for changes in cellular and protein content. This method of epidemiological research on poliomyelitis has been employed recently by Casey *et alii* (1945, 1946).

Mode of Transmission.

The evidence in favour of the mode of transmission of a disease is rarely clear-cut. It is difficult to establish without experiment absolute criteria of, for example, contact transmission as against enteric transmission. Furthermore, there may be more than one mode of transmission in one epidemic. In the absence of experimental evidence showing that only one particular mode of transmission of a disease is possible, one must submit all the data found in an epidemiological investigation to a consideration of each possible mode. In poliomyelitis the experimental evidence is not clear, and so it is necessary to consider the following possible modes of transmission: contact, enteric (including transmission by food and milk), animal, bird, insect vector *et cetera*. Our investigation showed us no evidence that transmission by animal, bird and insect vectors would explain the bulk of the data. We therefore eliminated all but enteric and contact transmission from consideration.

In attempting to establish whether a disease is transmitted by contact as against enteric means we would expect to find the following criteria in each:

Contact Transmission.	*Enteric Transmission.*
1. All cases should yield evidence of contact if sufficiently investigated.	Fullest investigation of each case need not show evidence of contact.
2. The disease is independent of the state of hygiene of the household and the method of sewage disposal.	The disease tends to accompany poor hygiene and unsatisfactory sewage disposal.
3. The disease is independent of the number of flies.	The disease tends to be associated with flies.
4. The urban incidence is higher than the rural incidence.	The rural incidence is higher than the urban incidence.
5. Evidence is lacking that the disease is associated with water, food or milk.	Evidence is found that the disease is related to water, food or milk.

Let us take these points in order.

1. In this epidemic the more fully we were able to investigate all contacts in a rural case, the more we found evidence of contact with a preceding case of paralytic or non-paralytic poliomyelitis. This applied also to the few urban cases which were investigated.

2. We could find no evidence, either rural or urban, that the incidence of the disease was related to hygiene. Many of the cases came from households with exemplary hygiene. The urban distribution (Figure II) showed no relation to the various sewerage districts. In any case, all but one of the urban cases came from the sewered areas, and only one from the surrounding small fringe of population living in unsewered areas.

3. Many of the households investigated had satisfactory fly screens, and in them flies were scarce.

4. The rural incidence was the same as the urban incidence.

5. We were unable, despite diligent inquiries, to connect the occurrence of the disease with food, milk or water.

In other sections further reference will be made to these points.

The evidence from the investigation was in favour of contact transmission. A number of examples illustrating this are shown in Figure V. The details of two of these series are shown in Figures VI and VIII.

The Incubation Period.

The term "incubation period" means the time interval elapsing between the time when the infective agent is implanted in a susceptible subject and the time of onset of the disease, as manifest by the first signs or symptoms. Not a great body of information is available on the length of the incubation period of poliomyelitis in man. The lower limit of the incubation period in experimental poliomyelitis induced by intracerebral and intranasal inoculation in monkeys and apes (rhesus, cynomolgus, chimpanzee *et cetera*) is of the order of six days. It appears reasonable that the lower limit of the incubation period of poliomyelitis in man is of the order of six days, although we realize the danger of accepting animal experiments as being an indication of the natural history of the disease in man.

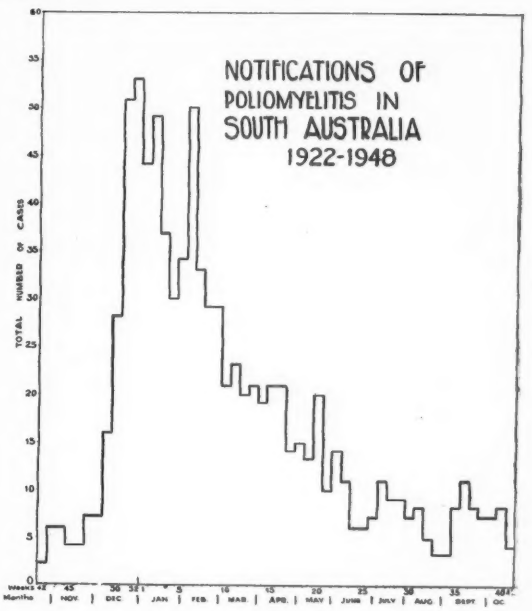

FIGURE IV.

In our investigations we discovered no case in which it could be stated that the infection was contracted from a single exposure of less than one day's duration. We have adopted a method of assessment of the incubation period that we believe to be valid. This concept is that when subjects are continuously in contact—for example, a family group—the interval between corresponding stages in successive cases—the "phase to phase interval"—is a measure of the incubation period. It is often difficult to decide what are the equivalent phases of illnesses. For our purposes we could attempt to analyse the time interval from onset of paralysis to onset of paralysis in successive paralytic cases; but as we have only four definite examples of these in our series we need something of more general application. Accordingly we considered that the most practicable feature would be the time of onset of the earliest prodromal symptoms. This we have called the "earliest prodromal date" (E.P.D.). Accordingly we have used the E.P.D. to E.P.D. interval as the most useful phase-to-phase assessment. There are at times difficulties in deciding on the E.P.D.

Normally in an infectious disease each earlier case would cause a number of cases to arise, as in Figure VII. The "scatter" of the second group of cases will depend on both the duration of infectivity in Case I and the normal variation in the length of the incubation period. For example, if in the figure above only Cases II and IX were known, then there would be a danger of assuming that Case IX had arisen from Case II, when in fact the cases are of common origin. One must therefore select

UNIVERSITY OF MICHIGAN LIBRARIES

some limits for the expected range of the incubation period, and the range that we have selected is six to thirty-five days.

When there were two possibilities, one of common origin and one of consecutive origin of a case, each interval being within the stated range for the incubation period, we have not accepted either of the possible figures for analysis.

The Bordertown series gives a simple example of phase-to-phase transmission (Figure VIII).

There is little information available on the time of highest infectivity in human, or even monkey, poliomyelitis. In man this is due to the fact that poliomyelitis

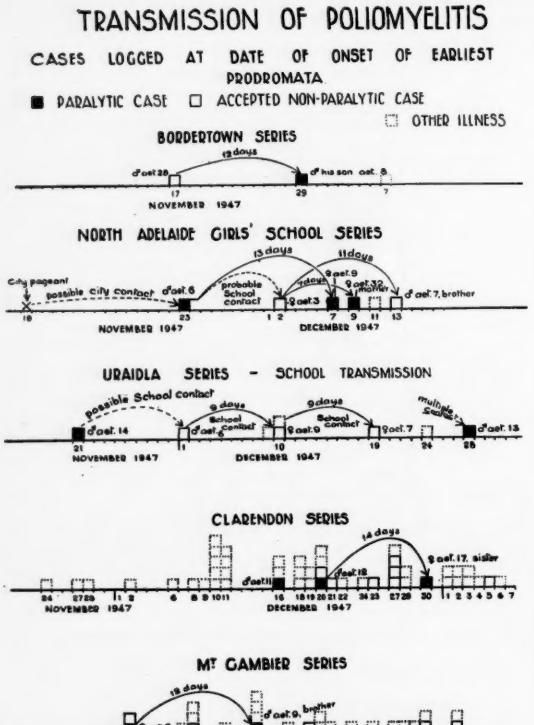

FIGURE V.

is a disease of apparently low infectivity—a statement which is confirmed for this epidemic by our studies on transmission in siblings and other contacts (see later). Taylor and Amoss (1917) have shown clearly in one case that virus can be isolated from naso-pharyngeal washings five days prior to the onset of symptoms. Virus has been obtained from naso-pharyngeal washings of paralysed and non-paralysed patients up to seven days after the onset of symptoms (Aycock and Kessel, 1943). The relation of E.P.D. to the time of infection of a contact is illustrated in Figure IX. The point *I* shown indicates the true time at which the patient in Case II contracted the infection from the patient in Case I. The true incubation period of Case II is the interval *I* to EPD_2, but is rarely known in man. When, as is usual, the relation of EPD_1 to *I* is not known, EPD_1 could be anywhere from *e'* to *e''*, so that it is possible for the observed phase-to-phase interval to be greater than, equal to, or less than the true incubation period, according to the proximity and the infectivity. The mean of a series of such observations has been taken as an approximation to the mean incubation period. We have sixteen rural and nine urban observations on the E.P.D. to E.P.D. interval. These 25 observations are analysed in Table IV.

We have attempted to use the data on the interval from E.P.D. to paralysis as a check on the data E.P.D. to E.P.D. intervals. Our other data on age and sex incidence and other evidence show no differences between the urban and rural poliomyelitis in this epidemic. Our data on the interval from E.P.D. to paralysis are given in Tables VA and VB and in Figure X.

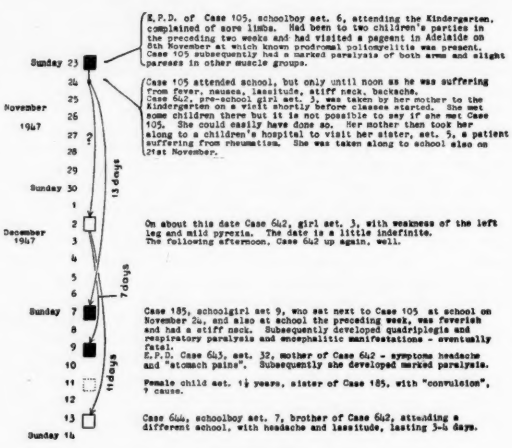
E.P.D. of Case 105, schoolboy aet. 6, attending the Kindergarten, complained of sore limbs. Had been to two children's parties in the preceding two weeks and had visited a pageant in Adelaide on 5th November at which known prodromal poliomyelitis was present. Case 105 subsequently had a marked paralysis of both arms and slight paresis in other muscle groups.
Case 105 attended school, but only until noon as he was suffering from fever, nausea, lassitude, stiff neck, backache. Case 642, pre-school girl aet. 3, was taken by her mother to the Kindergarten on a visit shortly before classes started. She met some children there but it is not possible to say if she met Case 105. She could easily have done so. Her mother then took her along to a children's hospital to visit her sister, aet. 5, a patient suffering from rheumatism. She was taken along to school also on 21st November.
On about this date Case 642, girl aet. 3, with weakness of the left leg and mild pyrexia. The date is a little indefinite. The following afternoon, Case 642 up again, well.
Case 185, schoolgirl aet 9, who sat next to Case 105 at school on November 24, and also at school the preceding week, was feverish and had a stiff neck. Subsequently developed quadriplegia and respiratory paralysis and encephalitic manifestations - eventually fatal.
E.P.D. Case 643, aet. 32, mother of Case 642 - symptoms headache and "stomach pains". Subsequently she developed marked paralysis.
Female child aet. 1½ years, sister of Case 185, with "convulsion", ? cause.
Case 644, schoolboy aet. 7, brother of Case 642, attending a different school, with headache and lassitude, lasting 3-4 days.
Sunday 23
November 1947
Sunday 30
December 1947
Sunday 7
Sunday 14
13 days
7 days
11 days

FIGURE VI.
The North Adelaide Girls' School series.

These means do not differ significantly, but a variance ratio test applied to the variances shows that these differ significantly ($P = 0{\cdot}02$). The two series therefore cannot be considered as a uniform collection of data.

As the rural cases were mostly investigated personally, whereas the urban cases were investigated mainly by postal methods only, it would be expected that in the urban series the earliest prodromata would tend to be overlooked by the family of the patient as being insignificant, particularly in the first case of a series, before attention was focused on the illness. We would therefore

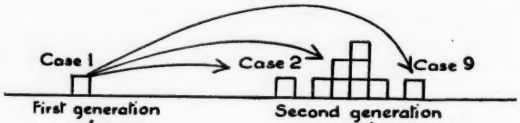

FIGURE VII.

expect the observations for both the E.P.D. to E.P.D. interval and the E.P.D. to paralysis interval to be longer in the rural series.

There is no correlation between the incubation periods and the interval from E.P.D. to paralysis.

The Roles of the Paralytic and Non-Paralytic Cases in the Spread of Poliomyelitis.

We have used the term "non-paralytic poliomyelitis" to indicate those cases in which were found some of the characteristic prodromal symptoms which occurred in the paralytic cases of our series. In the limited time at our disposal, we were able to find 60 of these cases. While closely investigating 14 paralytic cases in a small number of rural areas, we found 29 of these diagnosable non-paralytic cases, and because of this we have assumed that in this epidemic there were approximately two such non-paralytic cases for each paralytic case. As there were 103

paralytic cases, the true number of non-paralytic cases must have been considerably more than the 60 described. In fact, we excluded 12 cases otherwise suitable for inclusion in the analysis of the symptom incidence of the non-paralytic cases (five from Mount Gambier and seven from Clarendon), since they occurred in areas where it was considered that a mixed group of minor illnesses was probably occurring.

This brings up the wider question of the nature of non-paralytic poliomyelitis. There is little difficulty in deciding, in the presence of an epidemic, that a certain case is one

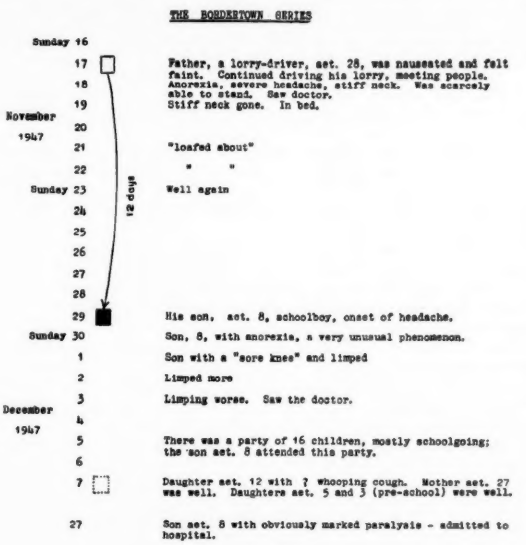

FIGURE VIII.
The Bordertown series.

of paralytic poliomyelitis. The problem lies in the diagnosis of non-paralytic poliomyelitis, and more fundamentally in the concept of the nature of non-paralytic poliomyelitis. How mild can an attack of non-paralytic poliomyelitis be, and how few symptoms need a patient show? Should the term "non-paralytic poliomyelitis" be extended, for example, to include a symptomless contact of a poliomyelitis patient, from whose pharynx or gut virus can be isolated?

In most human infectious diseases the presence of infection can be shown by (i) the occurrence of certain significant symptoms, (ii) the isolation of the infecting agent, and (iii) appropriate immunological tests. The only immunological test that has been developed for poliomyelitis is the neutralization test, which uses the monkey, and which is costly and time-consuming, and there is considerable doubt whether this test is specific for poliomyelitis. We were not able to use this test in our investigation, or the isolation of the virus. We had therefore to fall back on clinical criteria. In some areas we were able to account for the origin of nearly all cases by contact with preceding paralytic or non-paralytic cases (see Figure V).

FIGURE IX.

The answer to the question of how mild a case of non-paralytic poliomyelitis can be is of importance in assessing the proportionate roles played by the various sources of infection in the spread of poliomyelitis. If we accept that there are two diagnosable cases of non-paralytic poliomyelitis to each case of paralytic poliomyelitis, and if we assume that these non-paralytic and paralytic patients have equal infectivity and that these between them account for all transmissions, then we would expect about a third of the total of 103 paralytic cases to have had origin by contact with a preceding paralytic case. Turning to our observed figures, we have only two out of our 48 rural paralytic cases originating from an earlier paralytic case. There are three other rural cases in which there was possible or probable earlier contact with a preceding paralytic case—this would take our figure to a possible maximum of five out of 48. The less certain urban figures reveal only two, and a possible maximum of three, out of 55. These ratios differ significantly from the theoretically expected ratios of 16 out of 48 and 18·3 out of 55.

However, there is a feature which may account for some of the discrepancies. The number of further cases to which each type of poliomyelitis will give rise will depend on the extent to which the incapacitation due to the illness will remove the patients from circulation. In the paralytic cases the going to bed means that the patients will be confined there for some considerable time, until after they cease to be infective as far as contact (droplet) transmission is concerned. Our data on the interval between the E.P.D. and the date of confinement to bed are shown in Table VI and Figure XI. The modal value here is one day. These data indicate that, provided patients with paralytic poliomyelitis remain infective for two or three days after the onset of symptoms, there must be a substantial reduction in the transmission of infection if these paralysed patients are confined to bed. The patients with diagnosed non-paralytic poliomyelitis often did not go to bed, and if they did they were frequently up again,

TABLE IV.

Data on 25 Observations on the Length of the Incubation Period in Poliomyelitis, Classified into Transmission between Paralytic and Non-Paralytic Cases.[1]

Type and Distribution of Cases.	Days; Number of Cases.									Total.
	6	7	8	9	10	11	12	13	14	
Paralytic to paralytic, urban and rural	0	0	0	1	0	0	1	1	1	4
Non-paralytic to paralytic, urban and rural	1	1	1	1	0	1	3	0	1	9
Paralytic to non-paralytic, urban and rural	0	0	1	0	0	1	0	1	0	3
Non-paralytic to non-paralytic, urban and rural	1	1	0	2	0	2	0	2	1	9
Total	2	2	2	4	0	4	4	4	3	25
Rural, all transmissions	0	1	1	2	0	2	4	3	3	16
Urban, all transmissions	2	1	1	2	0	2	0	1	0	9
Grand total	2	2	2	4	0	4	4	4	3	25

[1] The mean of the 25 observations is 10·56 days. The mean of the 16 rural observations is 11·50 days. The mean of the nine urban observations is 8·89 days. The urban and rural means are significantly different ($P = 0·02$).

UNIVERSITY OF MICHIGAN LIBRARIES

TABLE VA.
Days Elapsing between Earliest Prodromal Date and Paralysis.

Group.	Days; Number of Cases.																Total.
	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	
Urban cases	2	6	10	6	9	6	4	5	2	1	0	1	0	0	0	0	52
Rural cases	2	6	8	6	5	2	4	4	3	1	1	0	1	1	0	1	45
Total	4	12	18	12	14	8	8	9	5	2	1	1	1	1	0	1	97

apparently well, the following day, but presumably still infective. Although we have no case in our series of a non-paralysed patient originating another case after apparently recovering from his symptoms, the reasoning appears sound.

TABLE VB.

Group.	Number of Cases.	Mean Period, E.P.D. to Paralysis.
Urban	52	3·93 days
Rural	45	4·54 days

The difference between the theoretically expected and the observed ratios of paralytic-to-paralytic transmissions does not appear to be satisfactorily explained by the evidence we have of the number of days during which the paralysed subjects were ambulant in relation to their ability to give rise to further cases.

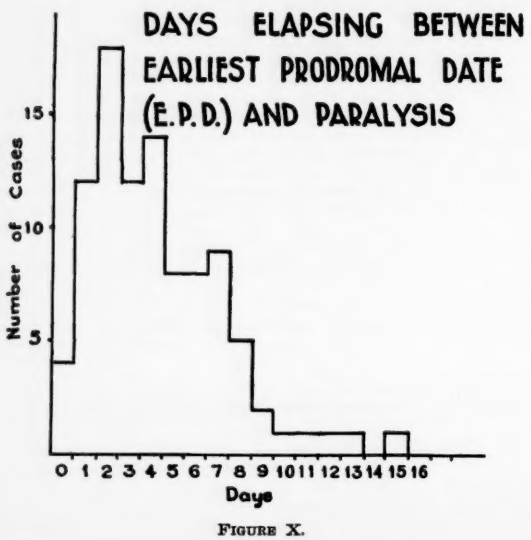

FIGURE X.

Until a larger series is investigated in this way it is not possible to make a final statement; but the evidence appears to indicate the presence of a number of infectors with few or no symptoms—that is, carriers. Where work has been done on detecting virus in healthy contacts of paralysed patients, the evidence appears to accord with this conclusion. Thus paralytic poliomyelitis can have origin by contact transmission from (i) paralysed patients, (ii) definable non-paralysed patients and (iii) ambulatory infectors whose illness is not diagnosable. Potentially group (iii), being unrestricted in activity, can give rise to the greatest relative number of cases if all three groups are regarded as equally infective for an equal length of time.

Age, Sex and Fatality Incidence.

Table VII shows an analysis of the age, sex and fatality incidence. The ratio of age to fatality incidence is shown in Figure XII.

The highest incidence rate of paralytic poliomyelitis in this epidemic occurs in the 49 to 168 months age group (four to fourteen years). Not only is the incidence rate high, but the death rate is significantly higher than in the rest of the population.

The probability of finding such an arrangement in a homogeneous population is 4·4% (that is, $P = 0{\cdot}044$).

If only the 73 to 96 months age group (six to eight years) is considered, in this the fatality rate is also significantly higher than in the remainder of the 103 cases.

The probability of finding such an arrangement in a homogeneous population is 3·6% (that is, $P = 0{\cdot}036$).

Of the 55 paralytic cases among males, nine were fatal—a fatality rate of 16·4%; of the 48 paralytic cases among females, eleven were fatal—a fatality rate of 22·9%; of the total 103 paralytic cases, twenty were fatal—a fatality rate of 19·4%.

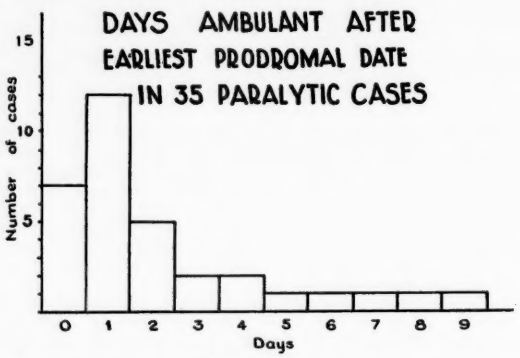

FIGURE XI.

There is no significant difference between the age incidence in the paralytic cases and that in the non-paralytic cases. In the paralytic series there is a strong indication that males predominate in the lower age groups (children), but not in the upper age groups (adults and adolescents).

The probability of finding such an arrangement in a homogeneous population is 7% (that is, $P = 0{\cdot}07$).

There has undoubtedly been a significant change in the age incidence of poliomyelitis from the time when epidemics of this disease first began to occur. All authorities are agreed that the changes are significant, but the reason for the age shift is not known. We were interested to see whether any change in age incidence occurred in the course of the 1947-1948 epidemic. The first and second halves of the series were compared. The analysis was made by comparing the number of persons aged less than fifteen years (that is, of any age up to fourteen years eleven months) in the population with those aged fifteen years and over.

It will be noted that in the second half of our series the number of adults has increased and the number of

children has decreased. An exact test of fitting shows that the probability of the arrangement of age classes in the table is only 10%. This is a strong indication, but not a definite conclusion, that there was an age shift during the course of this epidemic.

We have compared the age incidence in the paralytic cases of the 1947-1948 epidemic with figures available for the 1937-1938 epidemic. The figures for the 1947-1948 epidemic are ours. The 1937-1938 figures are from the records of the Central Board of Health of South Australia and are for all notifications, which include non-paralytic poliomyelitis and paralytic poliomyelitis, the great majority of cases being of the latter.

The age shift during the 1947-1948 epidemic is explicable by the theory that the public health and parental isolation of children decreased the transmission to those in the younger age group. For economic reasons isolation was more possible with children than with adults. This result is also in conformity with the contact theory of transmission of poliomyelitis.

TABLE VI.

Days Ambulant After the Earliest Prodromal Date in 35 Paralytic Cases.

Days.	Number of Subjects.
0	7
1	12
2	5
3	2
4	2
5	1
6	1
7	1
8	1
9	1
10+	1

The highly significant age shift between the 1937-1938 and the 1947-1948 epidemics may also be explained similarly, at least in part, but some alteration of the virus-host relationship is not excluded.

Transmission within Families and Households.

We wished to know how poliomyelitis was transmitted to family and other human contacts, for comparison with the usual incidence of an infectious disease which is greater in younger siblings. Table XIII shows our findings with siblings.

The attack rate found in this investigation is greater for older siblings (seven out of 24) than in younger (three out of 39). The difference is significant; with an exact test $P = 0{\cdot}029$.

Table XIV gives the transmission to all contacts, siblings and others, living in the same house as a paralysed patient.

Tables XIII and XIV show that in the rural personally investigated series we found that the maximum attack rate among domiciliary contacts including siblings was approximately 1 in 4 (30 out of 131), including both the accepted paralytic and non-paralytic cases and the possible non-paralytic cases listed. If we exclude the doubtful non-paralytic cases, the attack rate is 23 in 131, or approximately 1 in 6. When the investigation was made by postal means only, a much lower attack rate was found. In the case of the later rural series this lower rate (3 in 50, or approximately 1 in 17 domiciliary contacts) could be explained by the fact that these rural incompletely investigated cases occurred towards the latter end of the epidemic when one would normally expect a falling attack rate. However, the comparable finding for the attack rate (10 in 217, or 1 in 22) of the whole urban series shows that the difference was primarily due to the means by which the data were collected.

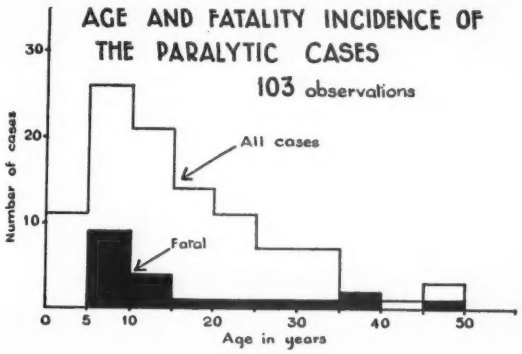

FIGURE XII.

Transmission within Schools.

There are several series which indicate unmistakably that transmission can occur within schools. The Uraidla series (Figure V) is largely one of school transmission. Another example has been given already in the North

TABLE VII.

Age, Sex and Fatality Incidences for Paralytic and Non-Paralytic Poliomyelitis.

Group.	Sex.	Age (Years). 0 to 1.	2 to 4.	5 to 9.	10 to 14.	15 to 19.	20 to 24.	25 to 29.	30 to 34.	35 to 39.	40 to 44.	45 to 49.	50 to 54.	Total.
Paralytic cases, urban and rural combined: First half ..	Male.	4	1	7	6	3	2	0	2	0	0	0	0	25
	Female.	1	1	9	4	4	2	2	2	1	0	1	0	27
Second half ..	Male.	0	2	9	7	3	4	2	1	1	0	1	0	30
	Female.	1	1	1	4	4	3	3	2	0	1	1	0	21
Total ..	Male.	4	3	16	13	6	6	2	3	1	0	1	0	55
	Female.	2 }6	2 }5	10 }26	8 }21	8 }14	5 }11	5 }7	4 }7	1 }2	1 }1	2 }3	0	48 }103
Fatal cases ..	Male and female.	0	0	9	4	1	1	1	1	2	0	1	0	20
Non-paralytic cases, urban and rural combined	Male.	1	10	7	3	2	3	2	2	0	0	0	0	30
	Female.	1 }2	4 }14	6 }13	7 }10	4 }6	2 }5	2 }4	0 }2	2 }2	0	1 }1	1 }1	30 }60
Paralytic and non-paralytic cases: grand total ..	..	8	19	39	31	20	16	11	9	4	1	4	1	163

UNIVERSITY OF MICHIGAN LIBRARIES

Adelaide Girls' School series (Figures V and VI). Since the school-going child belongs to the most susceptible age group, these results are not surprising.

Seasonal Incidence and Meteorological Factors.

Poliomyelitis is a disease which tends to have its maximal incidence towards the summer. That this is so for the South Australian notifications since 1922 is indicated in Figure IV. We consider that this predominantly summer incidence has been the main factor in the belief in enteric transmission of the disease that is entertained at least partly by a number of modern epidemiologists.

Table VIII.
Analysis of Ratio of Age to Fatality Incidence in the Paralytic Cases.

Outcome.	Age in Months.		Total.
	49 to 168.	1 to 48 and 169 to 600.	
Fatal	13	7	20
Not fatal ..	34	49	83
Total ..	47	56	103

We have analysed some of the records from the Meteorological Bureau of South Australia of the mean monthly absolute humidity and the monthly mean of daily maximum temperatures, but have not found a correlation between these meteorological factors and poliomyelitis incidence in South Australia over the period from 1922 to 1948.

Relationship to Water.

We inquired into the water supply of each household in which a case of poliomyelitis occurred. We could see no relationship between the poliomyelitis and the water supply. Figure II indicates the relationship between the water supply of Adelaide and the metropolitan cases of poliomyelitis. All the water mains in Adelaide are interconnected and the indicated distribution of water from the various reservoirs is only approximate. It can be seen from the figure that there is no significant grouping of cases in any particular water supply division.

Table IX.
Analysis of Ratio of Age to Fatality Incidence in the Paralytic Cases.

Outcome.	Age in Months.		Total.
	73 to 96.	Remainder.	
Fatal	5	15	20
Not fatal ..	6	77	83
Total ..	11	92	103

Relationship to Sewerage.

We could find no evidence that the distribution of the cases of poliomyelitis was related to the method of sewage disposal, either urban or rural. It will be seen from Figure II that all except one of the metropolitan cases occurred in sewered households in Adelaide. There was only one case that originated in the small fringe of unsewered households around Adelaide.

Relationship to Animals, Birds and Insects.

We inquired into the association of the poliomyelitis patients with animal and insect pests, domestic animals and birds, and the incidence of sickness in these, but found no significant relationship to poliomyelitis.

Relationship to Various Other Factors.

In our series there was no evidence that the incidence was related to pregnancy or childbirth. In our series of 103 paralysed patients, 48 were females, and 26 of these were of childbearing age. One patient who died, a woman, aged thirty-five years, had had a stillborn child seven weeks before the onset of poliomyelitis, and another woman who died had borne a child six months before.

Table X.
Analysis of the Age Incidence in the Paralytic Series.

Sex of Patients.	Age in Months.		Total.
	0 to 156.	157 to 600.	
Males	32 (61·5%)	23 (45·1%)	55
Females	20 (38·5%)	28 (54·9%)	48
Total	52	51	103

Two other women were pregnant, one three months and the other seven months, at the time of contraction of the disease. These do not appear to be an abnormal proportion for 26 women of childbearing age.

We could find no evidence of relationship to recent dental extraction or tonsillectomy. There were four patients who had had dental extraction in the six weeks prior to the onset of the disease, and only one patient had had a tonsillectomy in the previous six weeks. This patient, a girl, aged eleven years, had had a tonsillectomy fifteen days before the onset of poliomyelitis. It is of interest to note that two other children had had a tonsillectomy in the same operating theatre the previous day, and were nursed in the same ward, without evidence of poliomyelitis. It was soon after this that the existence of an epidemic of poliomyelitis was recognized, and very few tonsillectomies were performed in South Australia for some months.

Table XI.
Analysis of the Age Incidence of the 1947–1948 Epidemic—Figures from Our Own Series.

Age.	First Half.	Second Half.	Total.
Less than 15 years ..	33	25	58
15 years and over ..	19	26	45
Total	52	51	103

Table XII.
Comparison of the Age Incidences of the 1937–1938 and 1947–1948 Epidemics of Poliomyelitis in South Australia.

Age.	1937–1938.	1947–1948.	Total.
Less than 15 years ..	246 (72·6%)	58 (56·3%)	304
15 years and over ..	93 (27·4%)	45 (43·7%)	138
Total	339	103	442

$\chi^2 = 9 \cdot 8$, n = one degree of freedom, $P < 0 \cdot 002$.

Recommendations for Future Work.

We were handicapped by starting the investigation late in the epidemic. The preliminary stages of planning the method of investigation and of studying the early data in order to look for the most promising lines of investigation took about two weeks, which could have been better utilized had the preliminary work been done in the earlier

TABLE XIII.

Transmission of Poliomyelitis to Siblings Domiciled with a Paralysed Patient.

Families.	Number of Siblings Present.	Number of Families Containing These Siblings.	Siblings with Poliomyelitis.			Families Containing Affected Siblings.
			Paralytic.	Non-Paralytic.	? Non-Paralytic.	
Rural families:						
Younger siblings of the paralysed patient	39	21[1]	0	3	2	4[1]
Older siblings of the paralysed patient	24	11[1]	2	5	0	4[1]
Total	63	26	2	8	2	7
Urban families:						
Younger siblings of the paralysed patient	39	23[1]	0	3	0	1
Older siblings of the paralysed patient	31	19[1]	0	2	2	3
Total	70	35	0	5	2	4
Rural and urban families:						
Younger siblings of the paralysed patient	78	44[1]	0	6	2	5[1]
Older siblings of the paralysed patient	55	30[1]	2	7	2	7[1]
Grand total	133	61	2	13	4	11

[1] These figures do not appear to add; the reason is that some of the younger and older siblings occurred in the same family.

stages of the epidemic. In the field many data are obtained that will be lost if the field notes are long delayed in being converted into something more legible, hence expert stenographic assistance is essential. The finance and administrative arrangements must be adequate for the immediate following of likely epidemiological evidence, without one's having to wait for authority to proceed, as by the time a decision has been given the opportunity may have been lost. We were fortunate in being able to make decisions and put them into action immediately in the field.

SUMMARY.

An epidemic of poliomyelitis is described in which 103 paralytic cases occurred in the State of South Australia. The peak of the epidemic was in the summer of 1947-1948.

A brief history of the disease in general and in South Australia is outlined.

The epidemic was investigated from the epidemiological point of view. The methods of obtaining data by postal means, and the technique of interviewing patients and contacts in the field, are described.

Personal field investigation is necessary to obtain adequate knowledge of contacts and illnesses associated with paralytic poliomyelitis. Full and minute detail is essential for decisions on the nature of associated illness, possible transmissions of the disease, incubation period *et cetera*. These personal investigations were concentrated mainly on the scattered rural cases of poliomyelitis.

Many cases of non-paralytic poliomyelitis were found, only a few of these having been notified. Non-paralytic poliomyelitis is not easy to diagnose, and the diagnosis was made on epidemiological and clinical grounds. A statistical analysis of symptoms in sixty cases selected because of epidemiological and clinical findings establishes the symptom identity with paralytic poliomyelitis.

TABLE XIV.

Transmission of Poliomyelitis to Contacts Domiciled with a Paralysed Patient.

Series.	Contacts Aged Less than 50 Years.				Contacts Aged More than 50 Years.				Total, All Ages.				Number of Homes.
	Total.	Affected with Poliomyelitis.			Total.	Affected with Poliomyelitis.			Total.	Affected with Poliomyelitis.			
		Paralytic.	Non-Paralytic.	? Non-Paralytic.		Paralytic.	Non-Paralytic.	? Non-Paralytic.		Paralytic.	Non-Paralytic.	? Non-Paralytic.	
Rural and urban:													
Rural	173	2	21	9	8	0	1	0	181	2	22	9	41
Urban	204	0	9	1	13	0	0	0	217	0	9	1	54
Total ..	377	2	30	10	21	0	1	0	398	2	31	10	95
Personally investigated and not personally investigated:													
First 27, rural series, largely personally investigated ..	124	1	21	7	7	0	1	0	131	1	22	7	27
Last 14, rural series, not personally investigated ..	49	1	0	2	1	0	0	0	50	1	0	2	14
Total ..	173	2	21	9	8	0	1	0	181	2	22	9	41

UNIVERSITY OF MICHIGAN LIBRARIES

In certain areas which were the most fully investigated, we found that there were 14 paralytic cases and 29 accepted non-paralytic cases. We conclude that there are two diagnosable non-paralytic cases to each paralytic case.

The bulk of the evidence from this survey is in favour of the contact mode of transmission. There is no good evidence pointing clearly to other modes of transmission—for example, enteric, food, milk, animal or insect. The more time spent in investigation of a rural area, the more were all the transmissions discovered.

In the absence of data on the incubation period derived from single contacts over a very limited time, we adopted the concept that the phase-to-phase interval between successive cases of the disease continuously in contact approximates a mean incubation period. The phase-to-phase assessment used was that of earliest prodromal date (E.P.D.) to earliest prodromal date. This method yielded 25 observations, with a mean incubation period of 10·56 days.

In the paralytic cases the maximal incidence was in the five to nine years age group. The fatality rate was significantly higher in the six to eight years age group than in the rest of the paralytic cases.

It is shown that there is an age shift to a higher age incidence between the 1947-1948 epidemic and the preceding large epidemic of 1937-1938 in South Australia. This is an extension of the trend of the virus to attack later age groups than the infantile age distribution seen up to the beginning of this century. There is also a strong indication that a shift towards a higher age incidence occurred between the first and second halves of the 1947-1948 epidemic. It is suggested that the age shift is in part explained by public health and parental efforts to isolate the members of the younger age group in an epidemic.

The sex incidence (53·4% males in the 103 cases) was normal.

Among the household contacts, who were mostly siblings, we found evidence of an attack rate of between one in four and one in six, but very few of these developed paralytic poliomyelitis. The attack rate observed in older siblings was greater than that in younger siblings.

This evidence, and the lack of evidence of sufficient paralysed-to-paralysed transmissions, suggest that "ambulant infectors" or carriers occur apart from patients with diagnosable non-paralytic poliomyelitis.

Acknowledgements.

We wish to thank the following: the Crippled Children's Association of South Australia for financial aid originating this investigation; the South Australian Government for further financial assistance; the Committee on Poliomyelitis of the Faculty of Medicine of the University of Adelaide; the Central Board of Health of South Australia for data on this and previous epidemics; the Department of Lands and Survey of South Australia for maps; the Engineering and Water Services Department of South Australia for maps and data on water and sewerage; the Department of Anatomy and the Department of Physiology of the University of Adelaide for assistance; the Postmaster-General's Department for aid in preparation of the map of the urban incidence; Miss Gwen Walsh for preparing the maps and other text figures; the medical superintendent and staff of the Northfield Infectious Diseases Hospital; the medical superintendent and staff of the Adelaide Children's Hospital; the medical superintendent and staff of the Royal Adelaide Hospital; and private doctors for their records and assistance.

References.

Altmann, C. A. (1897), "An Epidemic of Fourteen (14) Cases of Acute Anterior Poliomyelitis", *Australasian Medical Gazette*, Volume XVI, page 173.

Aycock, W. L., and Kessel, J. F. (1943), "The Infectious Period of Poliomyelitis and Virus Detection", *The American Journal of the Medical Sciences*, Volume CCV, page 454.

Badham, J. (1836), "Paralysis in Childhood: Four Remarkable Cases of Suddenly Induced Paralysis in the Extremities, Occurring in Children, without any Apparent Cerebral or Cerebro-spinal Lesion", *London Medical Gazette*, New Series, Volume XVII, page 215.

Bertenius, B. S. (1947), "On the Problem of Poliomyelitis. An Epidemiological-Statistical Study", *Acta pathologica et microbiologica Scandinavica*, Supplement 68, page 1.

Blackall, P. (1904), "Epidemic Polyneuritis", *Australasian Medical Gazette*, Volume XXIII, page 347.

Casey, A. E. (1942*a*), "Observations on an Epidemic of Poliomyelitis", *Science*, New Series, Volume XCV, page 359; (1942*b*), "The Incubation Period in Epidemic Poliomyelitis", *The Journal of the American Medical Association*, Volume CXX, page 805.

Casey, A. E., Fishbein, W. I., Abrams, I., and Bundesen, H. N. (1946), "Relative Frequency of 'Subclinical' Poliomyelitis", *American Journal of Diseases of Children*, Volume LXXII, page 661.

Casey, A. E., Fishbein, W. I., and Bundesen, H. N. (1945), "Transmission of Poliomyelitis by Patient to Patient Contact", *The Journal of the American Medical Association*, Volume CXXIX, page 1141.

Caverley, C. S. (1894), "History of an Epidemic of Acute Nervous Disease of an Unusual Type", *Medical Record*, Volume XLVI, page 673; (1896), "Notes of an Epidemic of Acute Anterior Poliomyelitis", *The Journal of the American Medical Association*, Volume XXVI, page 1; (1914), President's Address, *Bulletin of the Vermont State Board of Health*, Volume XV, page 3.

Central Board of Health of South Australia (1922), Minutes and Correspondence, Number 149 of 1922.

Fenner, C. (1936), "The Geographical Background", in "The Centenary History of South Australia".

Ham, B. B. (1905), "The Recent Epidemic of Infantile Paralysis", *Australasian Medical Gazette*, Volume XXIV, page 193.

International Committee (1932), "Poliomyelitis. A Survey Organized by Jeremiah Millbank".

Litchfield, W. F. (1904), "The Recent Epidemic of Infantile Paralysis", *Australasian Medical Gazette*, Volume XXIII, page 346.

Stephens, H. D. (1908), "Summary of an Epidemic of 135 Cases of Acute Anterior Poliomyelitis Occurring in Victoria in 1908", *Intercolonial Medical Journal of Australasia*, Volume XIII, page 573.

Taylor, E., and Amoss, H. L. (1917), "Carriage of the Virus of Poliomyelitis, with Subsequent Development of the Infection", *The Journal of Experimental Medicine*, Volume XXVI, page 745.

Theiler, M. (1937), "Spontaneous Encephalomyelitis of Mice, a New Virus Disease", *The Journal of Experimental Medicine*, Volume LXV, page 705.

Theiler, M., and Gard, S. (1940), "Encephalomyelitis of Mice: I. Characteristics and Pathogenesis of the Virus", *The Journal of Experimental Medicine*, Volume LXXII, page 49.

Wade, R. B. (1904), "The Recent Epidemic of Infantile Paralysis", *Australasian Medical Gazette*, Volume XXIII, page 344.

Wickman, I. (1905), "*Studien über Poliomyelitis acuta; zugleich ein Beitrag zur Kenntnis der Myelitis acuta*"; (1913), "Acute Poliomyelitis", translated by J. W. Maloney, Nervous and Mental Diseases Monograph Series, Number 16.

IMPEDIMENTS TO PROGRESS IN MEDICAL EDUCATION.

By E. S. Meyers,
Brisbane.

Who shall decide when doctors disagree?
It is the solecism of power, to think to command the end, and yet not to endure the means.

Two interesting papers on the medical curriculum have appeared this year in The Medical Journal of Australia—one by Major-General F. Kingsley Norris, the past-president of the Victorian Branch of the British Medical Association, and the other by Dr. J. Kempson Maddox, this year's president of the New South Wales Branch of the British Medical Association. One would like to know to what extent the papers represent the views on medical education of the Councils of the respective Branches of the Association and of the Faculties of Medicine in Australia's most populous States.

In 1946, after several years' intensive study of the problem of the medical curriculum, a special committee of the Faculty of Medicine in Queensland published its report in a publication entitled "A Critical Review of Undergraduate Medical Training".

After the approval in principle of the report by the Senate of the University of Queensland, a start was made to change from the old to the new curriculum. Already, students who entered the medical faculty in 1947 have completed two years of study under the new curriculum and are now engaged in the work of the third year of a six-year course. This change from an old to a new curriculum, which would have been difficult in any circumstances, has been made even more so by the large number of students enrolling in the post-war years.

When the Faculty of Medicine was founded in 1936, plans were made on the assumption that at any one time there would not be more than 240 students in the course of six years. In point of fact, there were some who thought it would be many years before even this number would be reached. There are now some 550 medical students in the faculty.

Actual experience in bringing about curriculum reform and the opinions expressed in the two papers mentioned bring to mind the many difficulties encountered in effecting such changes.

"Setting the Course."

As far as one is aware, there is no body in Australia with functions exactly corresponding to the General Medical Council in England, to indicate as an instrumentality of the Legislature to the Australian universities the content and scope of undergraduate training in medicine. Furthermore, it is probably correct to say that in the various States there exists no statutory provision to ensure that there shall be regular reviews of the curriculum. Herein, then, is a difficulty to be overcome by those who desire that the curriculum should, according to changing circumstances, meet the needs of the community in respect of its medical service.

In 1947 the General Medical Council issued a booklet on recommendations as to the medical curriculum in Great Britain. In this booklet are set out the statutory position of the General Medical Council in regard to the medical curriculum, the objects of the recommendations and observations on new recommendations of the Council. There is no similar publication for the guidance of the various faculties of medicine in Australia. In many instances, improvements in the curriculum have come about solely as the result of the activities of an enthusiastic minority of graduates, of members of the university teaching staff and of medical students.

Another difficulty confronting those responsible for medical education in Australia is the present uncertainty of the shape of things to come in the medical practice of the future. It seems reasonable to believe that any revolutionary change in present conditions of practice would have a profound effect on methods of medical education. This question has received little, if any, attention from parliaments or universities.

Evidence exists to show that the several Australian medical schools have differing attitudes towards the various problems of medical education. This may be due, at least in part, to differing environmental conditions. For example, Kempson Maddox states that the aim of the undergraduate curriculum is no longer to produce a competent general practitioner. The Committee in Queensland stated as one of its desiderata that undergraduate training should enable graduates to practise general medicine and surgery skilfully; and Major-General Kingsley Norris says "attention should be directed to general practice rather than to the realms of the specialties".

The differences in outlook may be more apparent than real, as the written word does not always accurately express what one is thinking. There is, however, an aspect of the problem about which there should be no difference of opinion. Medical education is, or should be, a lifelong process and therefore some arbitrary limit must be placed on the content and extent of undergraduate medical education. The education of a doctor, however, should not cease at graduation. This will call for the provision of facilities for post-graduate medical education, not only for those who wish to engage in special work, but also for those who are to become general practitioners.

Four somewhat interrelated questions will now be considered—namely, better education of the student prior to entry into the faculty, matriculation, age of entry and reduction of the number of students entering the faculty. The following points are relevant to these questions.

1. Do the Australian faculties of medicine play any part in determining the type of education that should take place in primary and secondary schools? It is indeed paradoxical that students on completing their secondary education are generally well informed in physics and chemistry, but have in many instances no knowledge whatever of biology and sociology.

2. The governing bodies of the universities, not the faculties, are responsible for determining conditions of medical matriculation.

3. The age of entry into the faculty is also similarly determined.

4. In New South Wales and Queensland, Parliament determines that all who pass the matriculation examination must be admitted to the Faculty of Medicine should they so desire.

Some agreement and action by universities on these matters are desirable if medicine is to maintain its position as a learned profession.

The so-called "open door" policy in relation to the number of students entering the medical faculties has created many difficulties, and there is no doubt that it has militated against the early improvement in the curriculum that would have been possible with a smaller number of students.

Difficulties in Effecting Reform in the Pre-Clinical Years.

Physics, Chemistry and Biology.

Many candidates for matriculation in Queensland have studied physics and chemistry to senior standard. These subjects are now compulsory for medical matriculation. In the first year of the present medical course the study of these subjects is continued (physics for two terms and chemistry for three terms) with particular reference to their medical application.

It is thought desirable that all secondary school pupils who seek entry into the Faculty of Medicine should study biology also to senior standard. In fact, there has been a faculty recommendation that this subject also should be compulsory for matriculation. Educationists in England have similar ideas, not only in regard to those who are intending entering the medical faculty, but for all students. A text-book entitled "Social Biology" has been written for students in Great Britain by Alan Dale.

Anatomy and Physiology.

It is evident that there is a good deal of agreement that changes should be made in the teaching of anatomy and physiology. Evidence of this is seen in the papers of Major-General Norris and Dr. Kempson Maddox. The following items are noted: better correlation of teaching and the need for more attention to the anatomy of the living and applied anatomy; reduction in the number of didactic lectures; the need for more tutorial work; the need for more attention to be given to the study of the relationship of body and mind.

There are difficulties to be overcome in implementing these and other recommendations. It is said to be extremely difficult to interweave the teaching of anatomy and physiology, which is held to be possible only where there are on the teaching staff a number of experts in the various branches of the two subjects. A lead has been given in this matter by Professor Zuckermann of Birmingham (1947).

To teach applied anatomy of the living effectively, patients must be available for demonstration in close proximity to the anatomy and physiology lecture theatres. The study of the anatomy of the living requires accommodation of a kind not usually seen in anatomy departments—for example, a number of small rooms or cubicles with the necessary equipment for examination of the normal eye, ear *et cetera*.

As has been stated, far too little attention has been paid to the anatomy of the normal; but it is not possible to demonstrate to 100 or more students the anatomy of, say, the normal ear-drum, unless the facilities for teaching are available.

Much applied anatomy can be taught in a physiotherapy department, and it is unfortunate that far greater use is not made of this clinical material in teaching medical students; but here again adequate facilities must be available if the teaching is to be effective. Hospital departments, such as physiotherapy departments, have been planned as part of social service without due regard to the need of medical education, and as long as medical

UNIVERSITY OF MANITOBA LIBRARIES

education is looked on as a not very important by-product of a hospital service, teaching will never reach a high standard.

Teaching of mind-body relationship poses a real problem. Many students have no background whatever of biology, history or sociology. Many in high places in the academic world are critical of the student for his lack of culture, but give little help in securing for him the best that education has to offer. The students are thus often more sinned against than sinning. To a large extent responsibility for the students' attitude rest with those who prescribe the school and university curricula.

Major-General Norris rightly deplores the fact that the first introduction to anatomy is a corpse. It may be also said that the introduction and the greater part of the study of biology are upon the dissection of dead beasties, invertebrate and vertebrate. There is no study of behaviour in the invertebrate and vertebrate world, very little if any study of the instincts and the emotions and their importance as part of education.

One does not wonder, then, that Kempson Maddox considers that students take unkindly to the new unfamiliar world of the mind. Students like the obvious and simple, preferring to indulge the thalamus rather than exercise the cortex, keeping to the daily comic strip and the world of sporting events for preference. It is not suggested that these *divertissements* are quite out of place, but they represent far too frequently the limits of students' extra-curricular reading.

Dr. Kempson Maddox, like Major-General Norris, draws attention to the importance of the study of the living in regard to pathology. It is now many years since Lord Moynihan used the expression "pathology of the living". Surgeons seem to have given more attention to this subject than their medical colleagues.

There are a number of factors responsible for the divorce of pathology from clinical medicine. Possibly the most important one is that there has never been a happy marriage of the parties concerned. Pathologists are not often found in the wards of the hospitals (there is no doubt that they can give good reasons for their absence). It would be to the advantage of the student if the pathologist, with his colleague the physician or surgeon, conducted teaching sessions in the wards and out-patient departments of the hospitals. In fact, an intelligent appreciation of a large part of medicine and surgery depends so much upon an understanding of pathological processes in living people that one wonders why professorial pathological units do not exist in all teaching hospitals. It is a pity that the student's main impression of the pathologist is that he, too, is solely concerned with a corpse.

Medicine and Surgery.

The papers quoted bring to light many complaints about the teaching of medicine and surgery. Among them, then, one notes the following: too many didactic lectures; too great concentration on the specialties and the dismemberment of general medicine and surgery into more specialties; not enough attention to conditions that will concern students who will be the future general practitioners; not enough continuous study of disease processes throughout the full course of the patient's illness; not enough insistence that the patient is more than the sum of his parts, and that in far too many instances the human aspect of his problem receives no consideration at all; insufficient training in geriatrics and in chronic illness.

Major-General Norris draws attention, and rightly so, to the methods of clinical training that Professor J. C. Spence advocated when he was here. It has been the custom to leave much of the out-patient work in our large hospitals to the extremely hurried ministration of those who are not the most experienced teachers. If the methods that Professor Spence recommended can be introduced to Australian medical schools, there is no doubt that the effect will be to raise the level of the standard of teaching.

The formidable list of complaints that have been set down are evidence from those intimately connected with clinical teaching that hospital training is falling far short of what is needed.

Evidence is also available to support the teachers in the medical schools in their contention that all is not well with clinical training. The various medical students' journals and newspapers can add to the list of complaints, as will be noted later in this paper.

There will not be a true appreciation of these difficulties unless one considers some of the phenomena in the evolution of the Australian teaching hospitals. (i) The teaching hospital today is a multi-purpose hospital. (ii) Its outstanding activity, however, is specialty practice. (iii) The fields of general medicine and general surgery are becoming more and more circumscribed. (iv) Members of the staffs of teaching hospitals who have had even five years' experience in general practice are becoming progressively fewer. (v) All too frequently medical practice in out-patient departments of large teaching hospitals is by no means a model of the practice of medicine at its best. In many instances, as Major-General Norris says, "neither the responsibility to the patient nor to the student receives adequate consideration". (vi) The gradual disappearance of the general surgeon and the general physician is creating many problems in teaching. (This is not peculiar to Australia.)

A number of suggestions have been made for overcoming difficulties in teaching.

In some medical schools most of the undergraduate teaching is carried out in general medical and general surgical wards, and students visit special departments and wards only for set demonstrations. In the United States of America provision is made in many teaching hospitals for both undergraduate and post-graduate education. There are many resident medical officers of several years' standing who are responsible for much undergraduate medical teaching in general medicine and general surgery.

In Edinburgh some of the difficulties mentioned are overcome (according to a personal communication recently received from Professor Crew) thus:

> In order to teach Social Medicine as part of the whole of Medicine I have got a teaching general practice. Members of my staff serve under the National Health Service and run this general practice. They are headquartered on what used to be a public dispensary where medicine was prescribed for the poor, and now that everybody in this country can claim the services of his own doctor there are in this sense no poor and therefore the public dispensary system has become obsolete. I took over one of these dispensaries. We take batches of students every three months. The student is introduced to the home of the patient and, if acceptable, is given charge of that patient under supervision. In addition to the ordinary medical therapy he is required to do three things: to discover the role of any socio-environmental factor in the ætiology of the patient's condition; to trace the effect of the illness of this individual throughout the group to which the individual belongs—the family, the club, the factory and so on; and finally, with the aid of the almoner, to discover what social agencies exist which could contribute to the therapy, rehabilitation and final social resettlement of the sick individual.

It would appear that in order to prepare students for general practice it is necessary that they should receive training in hospitals other than the present teaching hospitals that are becoming more and more devoted to highly specialized practice.

Alternatively, teaching hospitals should provide many beds where patients are cared for by general physicians and general surgeons, provided these do not become extinct. There should be on the teaching staff a number of capable and experienced general practitioners.

It is very necessary that formal education of those who will enter general practice should not cease on graduation. In the immediate post-graduate period hospital instruction should be organized whereby the graduates will perform under supervision such procedures as come within the scope of general practitioners.

Obstetrics.

It is not easy to forecast the future of the teaching of obstetrics. Owing to changing social conditions, in Queensland at any rate, far more patients than formerly

not only go to hospitals for their confinements, but also are attended by their own doctors. With an increase in the number of students and a relative decrease in the percentage of the population in public hospitals, it would appear that we are faced with a problem that calls for urgent attention. It may be that we shall do as is being done in parts of America—namely, make use of the "clinical material" in private and intermediate wards. A visiting professor reported that this method was used in a large training school and that the patients very rarely made an objection except in the case of an odd millionaire or so.

It may be that history will repeat itself and that students will serve a term as apprentices to obstetricians in private practice.

Discipline and Recreation.

Kempson Maddox has drawn attention to disabilities affecting the student in the statement that "whatever syllabus is followed the first and second year student must have sufficient time to participate in the corporate life and recreations of the University. . . . Throughout his course the student must have leisure for reflection and for the digesting of one set of facts before another". The history of medical students' societies seems to indicate that too little attention has been paid to such problems.

Such criticism applies to student life generally. The elders in the community today may be divided into two classes: those who say (in public, frequently) that the youth of today have far fewer of the ethical virtues than at any time within memory, and those who say nothing but are engaged in one capacity or another in youth leadership.

What of the medical student as representative of one section of youth? It would require much statistical analysis (and this is a difficult matter when applied to human conduct) and the need to make adjustments (the old adage "other days other ways" being kept in mind) to make a comparison of medical students of this generation and the last. The important question is, how well are we, the teachers of today, shouldering our teaching responsibility? Our burdens press more heavily than those of our predecessors, since, apart from the difficulties already outlined, we have the outstanding problem of making adequate provision for the education of very large numbers of students.

As a result of experience one has come to believe that in directing the educational activities of the youth of today there is a need to exercise some measure of discipline and at the same time to realize the importance of giving help and encouragement. Furthermore, it is essential to appreciate the value of teaching by example instead of by precept alone, and of allowing the student to learn by doing. One feels that these methods should be followed by all concerned in the training of medical students. If it were possible, as Kempson Maddox suggests, one would like to see all students spending their eighteenth year in employment or in one of the services before entering the medical faculty. Many students today have had such experience, and in general their attitude towards their chosen vocation is better than that of the youth who comes into the medical faculty at seventeen or even sixteen years.

Some will object to discipline in the university; but unless all training is looked upon as discipline and care is taken to see that the conditions of training laid down by the faculty are satisfied, the student will lose much by the slackness of those who should maintain such discipline. Compulsory attendance at lectures is not considered an essential part of student discipline.

What is the method of determining that the student has honestly fulfilled the necessary discipline of practical training? Surely only the assessment by a competent judge of the constructive effort each individual has made —hence the need for an adequate number of teachers. Each student is required to carry out practical training in pre-medical and pre-clinical departments; but much of the value of such training is lost because many students have had little manual training. Each department of the faculty should have such a workshop where the student could be given manual training preparatory to carrying out experiments set out in his schedule of practical work.

One is informed that in one of the secondary schools in one of the States practical work carried out by pupils was much more efficient and effective than that of students in their first year at the university. The reason given for this was said to be that well-qualified technicians assisted in the practical instruction. Unfortunately there is a good deal of academic snobbery as to the relative importance of the work of the university teacher and the technician. This state of affairs did not apply in relationships between corresponding personnel in the services. The work of both is, of course, complementary, and a place should be found for selected technicians in the training of medical students.

The "Critical Review of Undergraduate Medical Training" previously mentioned states that "for a profession in which manual ability must always occupy a very high place, the lack of attention paid to this in undergraduate training is almost ludicrous". Germane to this question also is the following quotation from a letter by John Roberts in the *British Medical Journal*: "It is in the public interest that the future qualifying examination should evolve some means of eliminating the ambitious but ham-handed potential surgeon, however exalted his theoretic and academic attainments."

Linked with this question of training discipline is the need for a more rational system of examination—one in which more than memory is tested. For the better training of all the senses it should be possible to provide a better test to determine the eligibility of students to proceed to successive stages of the course and to graduation. It is not suggested that examinations should be abolished, as, human nature being what it is, without regular testing many students do not work.

There are many ways in which students may be helped. One does not refer to spoon-feeding, as no student can succeed unless he makes full use of his capacities and refrains from asking for help until he has made a genuine attempt to solve the problem in hand. It is, however, of the utmost importance that the student's burden should not be too heavy. He belongs to one of the few remaining groups who are required to work long hours night and day. Some teachers seem to think that the only way in which students can reach what they consider to be the Olympian heights of medicine, is by being confronted with tasks more difficult of accomplishment than the combined ascents of Pelion and Ossa.

Teaching by Example.

There are few gifted people who can impart lasting lessons merely by the spoken word in the so-called didactic lecture. It is doubtful whether even such people could succeed in a performance of such a type, repeated (even with some variation) up to 50 times. This type of teaching is seen at its worst in the lecturer who provides a most effective soporific in reading his postprandial lecture in the hours just past midday.

Clinicians have great opportunities of teaching by example and of imparting lessons that will last a lifetime. Those who were so fortunate as to sit at the feet of great masters of the art of clinical instruction in earlier times recall with what meticulous care the history was elicited, the orderly manner and the thoroughness of the physical examination, in the course of which each of the instruments of diagnosis that are at everyone's disposal—the eye, the hand, the ear and the nose—played its part, in order to demonstrate what was normal or what was abnormal in the various parts of the patient.

In these days of machine-made diagnosis and overspecialization there is a real danger that lip service only may be paid to these older training disciplines and that there will be fewer people competent to look after the ills that afflict the large majority of mankind. Is it our problem here that we are not prepared to give sufficient time to the history and the physical examination?

UNIVERSITY OF SYDNEY LIBRARIES

Learning by Doing.

Representative student opinion in most of the Australian medical schools is very critical of hospital training in the latter years of the medical course. At this stage the students are becoming weary of long years of irksome pupilage. They consider they should have the opportunity of learning by practice under supervision to carry out the variety of "minor" procedures which are an essential part of the everyday life of the general practitioner. It is claimed that many of such procedures are carried out in hospitals by nurses and wardsmen. Included in the work the students desire to carry out are the so-called "minor operative procedures"—surgical, gynæcological and obstetrical. Evidently the students do not agree that "they also serve who only stand and wait".

If the plans of the Faculty of Medicine become effective, medical students in Queensland will sit for papers in medicine, surgery, gynæcology and obstetrics at the end of the fifth year of the course. In the sixth year students will, it is proposed, act as apprentice resident medical officers. At the end of the sixth year they will be required to pass practical tests of the application of their knowledge to practical medicine.

Administrative Problems for the Faculty of Medicine.

Kempson Maddox is of the opinion that "the final design [of the curriculum] should be approved by the faculty and divorced from departmental or academic interests or routine university problems". It is not clear what is meant by this. It may mean that the Faculty of Medicine should be provided with its own pre-clinical and clinical departments solely concerned with responsibilities to the Faculty of Medicine. One does assume, however, that Kempson Maddox does not wish to divorce the medical faculty from the university, as he states in his paper that "medicine is not a separate entity, but exists as a part of the learning and culture of the times, of which culture the universities are the ultimate guardians".

The growth of medical schools, however, raises many problems; so does the growth of our universities; for example: "Is there an optimum size for a university?" "Is there an optimum size for a medical school?" "Should each university have a medical school on the university site?" "Should there be any change in the relationship of the faculties of medicine to the governing bodies of the universities?"

These questions have relevance to two important opinions held by those considered to be authorities on medical education overseas.

1. A modern medical school should consist of a building in which are housed a hospital and the various departments responsible for pre-clinical medical education — anatomy, physiology, pathology *et cetera*.

2. A modern medical school should be situated on the site of a university.

Other Problems.

Let us return to problems of the student. It has been seen there is general agreement as to the necessity for the future medical men to have a good general and professional education. There is also agreement, in principle at least, with Kempson Maddox, who stresses the need for students to have time for leisure and recreation and thought. Ideally these conditions are satisfied at places like Oxford and Cambridge, where one is told that the students do or did enjoy such an education, apparently spending the afternoons on the river or in some other delectable place.

In the United States of America medical students take a three-year college course leading to a bachelor of arts or bachelor of science degree and then proceed to the doctor of medicine degree after a four-years' medical course.

In Great Britain many students remain at school until they are eighteen or nineteen years of age before commencing their medical course of five or six years. Competent judges are of the opinion that such students are better informed and more mature than medical students in Queensland and possibly in other States as well. In Queensland the usual period of secondary education is four years. Many people believe that this does not allow sufficient time for general education. The majority of the students enter the medical course at the age of seventeen years. Thirty years ago most Queensland students did not commence their medical course in the southern States until a year later.

If secondary school students who are entering the medical course remain at school for another year or two, they will not be self-supporting until they graduate, which will be at the age of twenty-four or twenty-five years.

As has been pointed out earlier in this paper, the legislature is not very vocal on problems of medical education, although the Federal and State Governments do assist certain students to meet some of the costs. If it is assumed that the various faculties of medicine in Australia are in agreement that the period of secondary education calls for a course of study extending over at least five years, and that the length of the medical course should be six years, this important question arises: how are the costs of this prolonged period of education, including living costs, to be met? The burden weighs most heavily at present on people in the middle-income group who are excluded from receiving Commonwealth financial assistance by the means test.

Intimately connected with these financial problems there is another which has not been faced—namely, what is the number of medical practitioners required to meet Australia's needs in the near future? Included in Australia's needs are those of the territories for which Australia holds trusteeship.

Conclusion.

It would appear that the future training of our medical practitioners will be determined by three factors: (i) legislation enacted by Federal and State Governments; (ii) advice given by medical faculties and action taken thereon by the governing bodies of the universities; (iii) financial assistance available from governmental or other sources.

Reference.

Zuckermann, S. (1947), "Revision of the Anatomical Curriculum at Birmingham University", *The Lancet*, Volume I, page 395.

VARIANTS OF THE Rh TYPE: AN INTERESTING FAMILY STUDY OF AN Rh GENE ALLELOMORPHIC TO D.

By AILEEN M. DELANEY, B.Sc.,
From the Pathology Department, Brisbane General Hospital, Brisbane.

As a result of Levine's (1941) discovery of the anti-Hr (anti-c) serum, and also as a result of independent work by Race (Race *et alii*, 1944) and Wiener (1943), it became evident that the different Rh types are determined by the allelic genes, R_0, R_1, R_2, R′, R″, R_z and r. These genes are responsible for the production of corresponding antigens Rh_0, Rh_1, Rh_2 *et cetera*.

Having studied a table of reactions of four known Rh antisera with these seven antigens, Fisher (cited by Race, 1944) noticed that the reactions of one antibody were precisely opposite to those of another antibody.[1] He named the corresponding antigens C and c. Fisher postulated that the genes for these antigens were allelomorphic. The other two antisera were not antithetical and to their corresponding antigens he gave the letters D and E, and postulated the existence of their corresponding allelomorphs d and e. Competition existed between these two pairs as it did between C and c. Fisher supposed that the three genes representing the three selected antigens must

[1] Levine had also observed the antithetical nature of these two antibodies previously, but his results were not at the time available in England.

be situated closely together on the chromosome, since the combination is inherited as a single unit. The eight possible combinations of these three selected antigens corresponded to the seven antigens described by Race and include an eighth combination, CdE (Rh_7), which has now been found (Van den Bosch, 1948; Wiener and Hyman, 1948). The six most common chromosome assemblages, cDe, CDe, cDE, Cde, cdE and cde, correspond to Rh_0, Rh_1, Rh_2, Rh′, Rh″ and rh respectively.

Anti-e (anti-Hr″) was discovered by Mourant (1945), and Diamond (1946) and Haberman *et alii* (1948), by their discovery of the anti-d (anti-Hr_0), completed the series so brilliantly postulated by Fisher.

In 1945 the Rh group was still further subdivided by the discovery by Callender and Race (1946) of a third alternative or allelomorph at the C locus. This was called C^v and has been recognized in the combinations C^vDe and C^vde. Further allelomorphs at this locus, c^r and C^u, were later described by Race *et alii* (1948*a*). These were found in the combinations c^rDE and C^uDe.

In 1946 Stratton (1946), of Manchester, described a third allelomorph capable of existing at the D locus, and he called it D^u. Later, Race *et alii* (1948*b*), who tested samples of blood of genotype D^ud from 19 unrelated English people against 12 selected anti-D sera, demonstrated 12 different types of D^ud blood. Thus D^u was found to be not a specific variant of D, but rather a mosaic of closely related variants of this antigen.

Experimental Record.

A certain specimen of serum was recently sent to this laboratory to be tested for antibody specificity. The serum was from a patient (M.P.), aged twenty-five years (group A Rh negative), who was delivered of a normal male child in February, 1947, and of another male child on August 27, 1948. This second child (group A Rh_2) became jaundiced a few days after birth, but is now reported to be doing well, having had two blood transfusions, each of 110 millilitres, one on September 13 and a second on September 14. The patient (M.P.) denies any knowledge of ever having received a blood transfusion.

In the testing for specific antibodies, cells of the types Rh_1, Rh_2 and Rh″ were employed. Absence of reaction with Rh_1 cells and a positive reaction with Rh_2 cells suggested that a positive reaction should occur with Rh″ cells. But this was not the case. The test was then repeated with other Rh_1 test cells, and these gave a positive reaction with the serum. The Rh_1 cells (B.G.) used originally were those of a laboratory worker in this department. The serum was then tested against the cells of a group of 25 people of known genotype and again against B.G.'s cells. The reactions in general were as are set out in Table I.

TABLE I.

Rh Type.	Number of Samples Used.	Genotype.	Reaction with M.P.'s Serum.
Rh-negative	5	cde/cde.	Negative.
Rh′	1	cdE/cde.	Negative.
Rh_0	1	Unknown.	Positive.
Rh_2	1	cDE/cDE.	Positive.
Rh_1	4	CDe/CDe.	Positive.
Rh_1	6	CDe/cde.	Positive.
Rh_1Rh_2	7	CDe/cDE.	Positive.
Rh_1 (B.G.)	—	CD^ue/cde.	Negative.

Failure of the serum to react with Rh-negative cells eliminated the possibility of the presence of agglutinins against c, d or e. Similarly, failure to react with Rh″ cells showed the absence of anti-E. Positive reactions with homozygous Rh_2 cells (having no C) and the other Rh_1 cells used indicated that it was a variant of the antigen D in B.G.'s cells that was causing this unusual reaction.

As no source of Rh′ (Cde/cde) cells was available here to eliminate the posibility of any anti-C being in the serum as well as anti-D, a sample of M.P.'s serum was forwarded to Mr. R. T. Simmons, of the Commonwealth Serum Laboratories, Melbourne, who was kind enough to test it against his Rh′ test cells. He found that the serum contained no agglutinating antibody anti-C. He was able to show by means of a series of 16 known anti-D and anti-D D^u test sera that this D variant in B.G.'s cells was not identical with Stratton's D^u, but, nevertheless, was closely related to it. The serum of M.P. was shown to be an anti-D serum without any anti-D^u.[1]

The collected information was forwarded to Dr. R. R. Race for his comments, and he considered from it that the D in B.G.'s cells was different from the usual D generally found.

Discussion.

A feature which became evident during this investigation was the necessity and value of having available cells from a group of people of known genotype. The Rh″ and homozygous Rh_2 test cells proved to be most useful in this particular study. In the establishment of our panel of known cells every assistance has been given to this department by the Commonwealth Serum Laboratories.

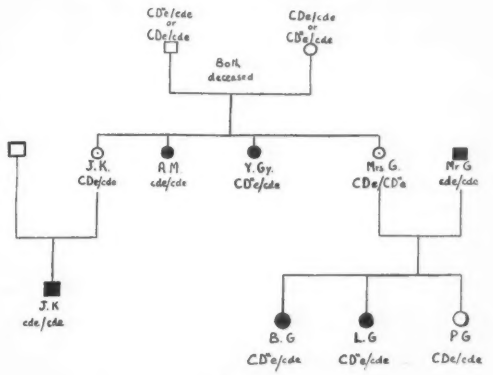

FIGURE I.

The circles represent females, the squares males. Black circles and squares represent those M.P. negative, white circles and squares those not tested and white circles with a central dot those M.P. positive. Mrs. G. is M.P. positive because her cells contain ordinary D as well as D^u. At first sight a wrong impression might be gained from the part of the figure dealing with Mr. G. and his family; it might appear that the inability of the cells of two daughters of Mr. G. to react with M.P.'s serum has been inherited from him, but actually his cells are M.P. negative simply because they are Rh negative.

It must be emphasized that the possession of a panel of cells of known genotype is of more than academic interest. Indeed, such a panel is necessary to assess correctly the specificity of any anti-Rh serum found in a patient. It will be recalled that for most clinical purposes it is sufficient to know whether a patient is Rh-positive or Rh-negative without a knowledge of his sub-type or genotype. By Rh-positive is meant that his red cells possess the D antigen, and so, if Rh-negative, he will lack the D antigen in his red cells. To classify a patient in this way, of course, requires anti-D serum, so that it is obvious that the clinician or laboratory worker must have issued to him anti-Rh serum of anti-D specificity. It is clearly impossible to assess the exact specificity without the panel of "key" cells.

It is because of this that it is essential that any anti-Rh serum discovered be forwarded to a central laboratory suitably equipped by virtue of personnel and material to ascertain the antibodies present in the serum. This laboratory can then direct the serum into the most useful channels for the maintenance of supply of this precious commodity, for which there is an ever-increasing demand.

[1] Of "anti-D" sera over 50% contain both antibodies, anti-D and anti-D^u. The remainder contain no anti-D^u.

The existence of the D^u variant of D described in this paper further illustrates the necessity of sending anti-Rh sera to specially equipped centres for assessment of their specificity. If the serum of M.P. was used as an anti-Rh serum for routine testing, it would classify as Rh-negative certain D^u cells. The frequency of D^u is at present unknown and admittedly must be low. However, to quote a particular case, B.G. would be classed as Rh-negative by serum M.P. and so might be used as a donor for an Rh-negative individual.

The finding described above is interesting, not only from the point of view of its being the first variant of D reported in this country, but also because of the perfect segregation which has been found to have taken place in B.G.'s family. The information obtained from tests on this family is revealed in Figure I.

It was thus possible to work out the genotypes of B.G.'s grandparents although they were deceased. Nicely enough, these grandparents have expressed in their four children the four possible combinations of the chromosomes concerned with Rh inheritance. Also it is fortunate that Mr. G. is Rh-negative, thus allowing the D^u or other variant of Mrs. G. to be freely expressed in the selected offspring. The value and accuracy of blood gene inheritance studies in families are thus demonstrated.

Summary.

An example of the D^u variant of the D (Rh_o) antigen in human red cells is described. It is of interest because, firstly, it is the first report of such a variant in this country and, secondly, because of the interesting family tree.

The genealogy is described and discussed, and the part played by D^u in the Rh system is also discussed.

Acknowledgements.

I wish to thank Mr. N. R. Henry, of this laboratory, for his interest taken in this investigation and for his advice given throughout it. I am grateful also to Dr. J. V. Duhig, director of this department, for permission to publish this paper. Thanks are also due to Mr. R. T. Simmons (Melbourne) for extensive laboratory tests, to Dr. J. O'Reilly (Sydney) and to Dr. R. R. Race (London) for their generous assistance. Finally, I should like to thank the members of the family concerned, who were so helpful in making this investigation possible.

References.

Callender, S. T., and Race, R. R. (1946), "A Serological and Genetical Study of Multiple Antibodies Formed in Response to Blood Transfusion by a Patient with Lupus Erythematosus Diffusus", *Annals of Eugenics*, Volume XIII, page 102.

Diamond, L. K. (1946), "Physicochemical and Immunological Character of Rh Antibodies", paper read at the International Hæmatology and Rh Conference, Dallas, Texas, November 15, 1946.

Haberman, S., Hill, J. M., Everist, B. W., and Davenport, J. W. (1948), "The Demonstration and Characterization of the Anti-d Agglutinin and Antigen Predicated by Fisher and Race", *Blood*, Volume III, page 682.

Levine, P., Burnham, L., Katzin, E. M., and Vogel, P. (1941), "The Role of Iso-Immunization in the Pathogenesis of Erythroblastosis Fetalis", *American Journal of Obstetrics and Gynecology*, Volume XLII, page 925.

Mourant, A. E. (1945), "A New Rhesus Antibody", *Nature*, Volume CLV, page 542.

Race, R. R. (1944), "An 'Incomplete' Antibody in Human Serum", *Nature*, Volume CLIII, page 771.

Race, R. R., Sanger, R., and Lawler, S. D. (1948*a*), "Rh Genes Allelomorphic to C", *Nature*, Volume CLXI, page 316; (1948*b*), "Rh Genes Allelomorphic to D", *ibidem*, Volume CLXII, page 292.

Race, R. R., Taylor, G. L., Cappell, D. F., and McFarlane, M. N. (1944), "Recognition of a Further Common Rh Genotype in Man", *Nature*, Volume CLIII, page 52.

Stratton, F. (1946), "A New Rh Allelomorph", *Nature*, Volume CLVIII, page 25.

Van den Bosch, C. (1948), "The Very Rare Rh Genotype R_{YI} (CdE/cde) in a Case of Erythroblastosis Fœtalis", *Nature*, Volume CLXII, page 781.

Wiener, A. S. (1943), "Genetic Theory of the Rh Blood Types", *Proceedings of the Society for Experimental Biology and Medicine*, Volume LIV, page 316.

Wiener, A. S., and Hyman, M. A. (1948), "Observations on the Rare Genes R^z and r", *The American Journal of Clinical Pathology*, Volume XVIII, page 921.

SYPHILIS RESURGENS.

By E. H. Molesworth, M.D., F.R.A.C.P., Dip. Rad.,

Honorary Member of the Royal Society of Medicine (Dermatology), London; Consulting Physician, Diseases of Skin, Royal Prince Alfred Hospital, Sydney.

The problem of syphilis is one in which I have been intensely interested during the whole of my professional career. When I was a student, patients with syphilis at Royal Prince Alfred Hospital were unwelcome, and drained into the surgical out-patient department, though the surgeons did not want them. This aversion was justified, because very few diseases present fewer developments which call for surgical intervention than does syphilis. When, therefore, the skin department showed interest in these patients, and wanted to undertake the treatment of them, there was practically no opposition.

Fortunately, at that moment the new arsenical drugs became available for use, and the principal difficulties experienced were those attendant upon the provision of regular, as well as adequate, treatment with those drugs. I think I can say without fear of well-founded contradiction that I was the originator of the idea of establishing evening clinics. At first this was strongly opposed on two grounds: (i) that if evening clinics were established for venereal diseases, the demand for similar provision for all other diseases would arise and be very difficult to combat; (ii) that the established and hitherto unchallenged belief that mercury was the best treatment for syphilis (and one which could be carried on without the patient himself attending personally once a week over a long period) was being jettisoned in favour of the new-fangled and unproven drug, the administration of which demanded the personal attendance of the patient, because it had to be injected intravenously.

As at that juncture the intravenous injection of "Salvarsan" was combined with the intramuscular injection of mercurial preparations, this objection was easily combated, though the new treatment required the attendance of the patient once weekly at least for the combined treatment by arsenic and mercurial drugs.

This weekly attendance was, for the vast majority of patients, impossible without a grave risk to the permanence of their employment, if they had to leave their jobs for half a day each week for months on end. However, if they were given the opportunity of attending for treatment after working hours, there would be no valid excuse for absenteeism.

How we overcame the very strong opposition to the establishment of evening clinics for the treatment of syphilis (and gonorrhœa, in which the skin department had no interest) is a long and old story into which I do not mean to go in this paper. But we did overcome it, and the first clinic instituted was at the Royal Prince Alfred Hospital. This soon became so overcrowded that we had to send out an "S.O.S.", to which Sydney Hospital and the Board of Health replied.

To give medical men of recent graduation an idea of the frequency of syphilis in those days, I can only refer to the fact that I and my contemporaries as students during the first decade of this century used to see each week in the surgical out-patient department from three to seven new patients with early primary and secondary syphilis, not to speak of numerous old patients under oral treatment with mercury or potassium iodide, or both. The total can be imagined by reference to a British Royal Commission, which after a long survey of the situation in the British Isles, reported (in 1910, I think), as its deeply considered opinion, that 10% of the population of all large cities (especially seaports) had or had had syphilis.

In addition, I can well remember that, aided by a resident and two or three nurses, I personally gave intravenous injections of "Salvarsan" to between 30 and 40 patients on each occasion that the evening clinic was open. This was no mean feat, when it is remembered that with

the old "Salvarsan" it was necessary to dissolve the drug in 100 to 150 millilitres of sterilized normal saline and to render the solution alkaline by adding caustic soda solution until the precipitate formed was redissolved. This alkaline solution was transferred to a container hung about two feet above the point of injection. The needle was then inserted into a vein and the solution was allowed to run in by gravity, but the flow was checked by a clamp on the rubber tube (connecting the container to the needle) just at the moment when the last of the dose left the glass container. Normal saline was then poured into the container and the clamp was removed until the drug remaining in the rubber tube was run into the vein by the following saline solution.

I remember that we had four couches and about eight sets of apparatus. The job was done like mass production in a modern factory. One nurse took out the injected patients in turn and brought in a new one to the vacated couch. Another nurse rubbed ether on the antecubital region and applied the tourniquet. A sister was in charge of the sterilizing, taking down the used apparatus, putting it into the sterilizer, and substituting a fresh one filled with a new dose of "Salvarsan" solution. On her heels I came, put the needle into the vein, removed the tourniquet, slackened the clamp on the rubber tube, saw that the solution was running into the vein and not into the subcutaneous tissue, and moved on to the next patient. I was followed by the resident medical officer, who saw to the completion of the injection, removed the needle and gave the patient a swab of cotton wool to press on to the puncture until the first nurse came to him, removed the cotton wool, dabbed a patch of strapping on the area and took him out.

Thus we went round and round until all the patients had been treated. With a preliminary examination to decide which patients were to receive an intravenous injection, and which to receive an intramuscular injection (then of mercurial cream), the whole business took from 7 p.m. to 9.30 p.m. even when organized as above.

Later, when the "Neo-kharsivan", "Novarsenobenzol", "Novarsan" preparations came into production and use, each dose soluble in 10 millilitres of distilled water and injected by a syringe, the procedure was much simplified. The sister filled the syringe and handed it to the operator, who attached the needle, put the latter into the vein, injected the dose, withdrew the needle, handed the syringe and needle back to the sister for sterilization, received a freshly-charged syringe, attached a new needle and proceeded to the patient on the second couch. As soon as the resident medical officer became expert in finding the vein he was, of course, encouraged to inject as many patients as he liked, and that saved a lot of time. But even then, the clinic rarely finished under two hours.

Men on night work or women who preferred to attend by day were treated by the resident medical officer. Even at the pace described, with clinics on two evenings each week, we could not cope with the numbers of applicants for treatment.

The institution of compulsory notification of patients infected with syphilis (by number, not by name) certainly helped, though I must confess that I was not enamoured of this project at first, on account of the implied breach of confidence between doctor and patient. But I must admit the measure was very helpful in ensuring regular attendance by the careless or sceptical patients for the prolonged periods required for probable cure.

These evening clinics—first established, I think, about 1911 or 1912—went on, full steam ahead, up to, during and after the 1914-1918 war, though in the early part of the war period substitutes for the German "Salvarsan" had to be used. Before the end of the war, however, English "Kharsivan" and French "Arsenobenzol" were available, and the "neo" varieties soon followed. Not only were these "neo" varieties (now grouped together as neoarsphenamine) much quicker to prepare and simpler to inject, but the quantity of fluid being much less (10 millilitres as against 200 millilitres with the older varieties) caused much less sickness on the part of the patients. Full doses of neoarsphenamine (0·9 gramme for an otherwise healthy adult of 10 stone or more) were very well tolerated, provided a watch was kept for albuminuria or other toxic symptoms.

At first the treatment, by intravenous injections, of syphilitic patients in the out-patient department was criticized, but when it was shown that no ill effects followed such procedures it became the general practice to treat patients with uncomplicated syphilis as ambulant patients.

In the earlier days, a certain small proportion of patients treated by the arsenical drugs showed severe toxic signs like exfoliative dermatitis, and a very few showed signs of dangerous hepatic intoxication. Very soon, however, these were shown to be due to too frequent repetitions of the dose rather than to the magnitude of the individual dose. When this was realized, toxic manifestations as described above practically disappeared from the records of the Royal Prince Alfred Hospital, the only examples occurring being among patients who had been treated outside the institution and not according to the rules laid down in the Royal Prince Alfred Hospital syphilis clinic.

Next came the substitution of bismuth preparations for the mercurial injections. Bismuth, given by intramuscular injection, was found to be at least as effective as mercury and much less toxic. So mercury was deposed from its originally proud position as the first drug for choice in the treatment of syphilis to a position of little importance (third in those days, and now, with the advent of penicillin, not higher than fourth).

Under this regime (intravenous neoarsphenamine and intramuscular bismuth injections) great progress was made; patients gained confidence and absorbed the doctrine that early treatment by these methods meant early and complete cure, the infective period of each patient was enormously reduced, and fresh infections became fewer and fewer, until by 1930 patients with primary and early secondary syphilis became so very rare that, up to the beginning of the recent war, it was very difficult to find more than one or two such patients *per annum* for the purpose of demonstration to students.

Incidentally, I cannot subscribe to the grouping of early cases of syphilis as "acute syphilis". Most of these are chronic even in the early stages, and the term "acute" syphilis, in my opinion, should be reserved for the fortunately rare examples that used to be called "malignant" syphilis.

There was a mild "kick-up" in the curve of incidence of the disease after a visit here by an American fleet before the 1939-1945 war.

During the period of falling incidence in Australia, a similar but not as great a fall was experienced in Europe (according to personal inquiries in England and Germany in 1927, and to correspondence and medical literature). The one civilized country that lagged behind was the United States of America. Whatever may have been the cause of this—mixed races and especially a large, careless, negro population providing a nidus of infection, failure to introduce universal compulsory notification of syphilis, some defect of treatment (mass or individual)—the fact remains that at the outbreak of the recent World War the incidence of syphilis in the United States of America was very heavy as compared with Europe, and enormous as compared with Australia. This soon became apparent when United States troops came to Australia in considerable numbers in the last two-thirds of the recent war. Of course, it is well known that in war time there is always a slackening of sexual morality. On this ground I had hoped that the large increase of infections would disappear soon after the war ended. But unfortunately these hopes have not been fulfilled. Of course a fresh nidus has been formed by infection brought here by American troops, but alarming as it is, as shown recently in the public Press on figures obtained from the Health Department, it is quite small as compared with the incidence at the time when I was a student and a young member of the staff of the Royal Prince Alfred Hospital between 1904 and 1920. And, according to Dr. J. Cooper Booth's figures, it is still increasing. It would strain my credulity to breaking point to believe that the sexual morality of the younger people of today is notably slacker than among a similar age group in the early years of this

century. It is true that there has been some noticeable slackening of parental control, especially of girls, and it is probable that the diminished fear of infection, owing to escape from contamination during the period 1926 to 1942, may be a minor factor, but I cannot believe that the real standard of sexual morality is lower today than it was between 1926 and 1942.

Today there seems to be a much smaller number of professional prostitutes than in the first quarter of this century, but I am interested to note that Dr. Cooper Booth finds that the majority of recent infections with syphilis today can be traced to the enthusiastic amateur and that only a small proportion of such infections derive from the professional prostitute. But exactly the same observations were made by me (Molesworth, 1916) many years ago. This again is evidence that relaxation of sexual morality, especially on the part of the female section of the population, is not sufficient to explain the increase in the incidence of syphilis in Australia today, any more than a supposed tightening of the code of sexual morality between 1926 and 1942 can be held responsible for the very great fall in the incidence of syphilis during that period.

Yet, through the whole duration of the recent war and right up to the present moment, there has been no shortage of arsenical and bismuth drugs for the treatment of syphilis. There has even been an additional drug, potent at least in clearing visible signs of the disease. This, of course, is penicillin. In spite of this, however, we are slipping back and back since the good period, 1926-1942.

The introduction of fresh infection by American troops explains this state of affairs at least in part, but at its worst the incidence of syphilis today, though alarming, is hardly comparable with the incidence when the arsenical drugs were introduced about 1910. Yet, with the earlier varieties of the arsenical drugs (let us call them arsphenamine and neoarsphenamine) aided by bismuth, this much larger incidence was reduced by the third decade of the nineteenth century almost to vanishing point.

Another very probable source of fresh infection is the large numbers of European refugees who arrived here from 1932 to 1940. During the war more refugees arrived from Indonesia and other areas north of Australia. Since the war there has been a further abnormally large influx of immigrants from Europe. Among these there were probably an appreciable number with latent syphilis. All these sources, not only the infected immigrants themselves but the people infected by them, have no doubt increased the incidence of syphilis. This probably explains Dr. Cooper Booth's observation that the upward trend of the curve of incidence began before the American troops came to Australia in large numbers.

What then can be the reason for failure of anti-syphilitic treatment since 1945? Are the younger generation today less moral in the sexual sense than that corresponding age group between 1920 and 1936? Have our evening clinics fallen into disuse? Has the notification of the disease become slack? Are the drugs used today less effective? Are the methods of administration of treatment less effective than the methods employed earlier?

I have already expressed my strong conviction that the modern youth is not less moral in the sexual sense than their corresponding age group between 1920 and 1936. As for the present conduct of the evening clinics, I cannot answer—at least from personal experience. Perhaps someone else can do so.

Then as to the notification question, Dr. Cooper Booth's figures are based upon cases notified in recent years. It would, therefore, appear that this is not a potent factor in the recent increase in the incidence of syphilis. There remains, therefore, the consideration of the drugs used today, and of the manner of their use. It is undoubted that the treatment responsible for the rapid decrease of syphilis (1920-1935) was the intravenous administration of maximum doses of arsphenamine and neoarsphenamine, together with the intramuscular injection of bismuth. I think that the giant's share of the credit was due to the intravenous injection of the arsenical drugs mentioned. Yet I find that these are almost entirely discarded today in favour of intramuscular injections of "Acetylarsan" (Board of Health clinic) and of "Mapharsen" given by the intravenous route in other clinics.

I suggest that the success of the earlier arsenical drugs was due to the shock tactics adopted in their administration (intravenous). Treponemata in the circulation and in the more vascular tissues were suddenly subjected to a very strong concentration of the drug and destroyed. The drug, however, is quickly eliminated, and a proportion of the surviving organisms would drift out from their hide-out in tissues with scanty blood supply into the circulation. These would be met a week later with a fresh flood of the drug. This would mean that fewer and fewer treponemata survived after each injection and, some induced immunity having been developed, probably the drug and acquired immunity together were able to eradicate entirely the infective agents. That this actually did occur is shown by the sharp decline of the incidence of syphilis, the hitherto unknown occurrence of second infections, the practical disappearance of congenital syphilis and the (later) sharp diminution in incidence of *tabes dorsalis*, general paralysis of the insane and other involvements of the central nervous system. This fact comes from practising psychiatrists, and particularly from Dr. J. A. McGeorge and Dr. C. H. Swanton.

I am informed by physicians that cases of cardiac involvement, aneurysm and other syphilitic diseases of the arteries and circulatory system have become very rare.

Latterly, however, the technique of treatment has altered. In the use of "Mapharsen", the idea seems to be to repeat the injections so frequently that the drug is kept as nearly as possible at saturation in the circulation. The effect of this, I suggest, is to keep a proportion of treponemata alive but viable in the less vascular tissues. They hibernate, so to speak. But being subjected in their retreat to insufficient doses of the drug, they become arsenic-resistant and can finally survive concentrations of the drug that are ample to destroy non-arsenic-resistant treponemata.

This was known to occur before ever arsenical drugs were used to treat syphilis. When various arsenical compounds were used to treat trypanosomiasis in man and animals, it was found much better to subject the trypanosomes to intermittent shock doses of these drugs. This, I suggest, is a potent cause of the recrudescence of syphilis today. This method originated in the United States of America, but as I mentioned above, the control of syphilis in that country fell far behind the standard attained by the rest of the civilized world between 1910 and 1935. Much as I admire other aspects of medical work in the United States of America, I am not prepared to bow the knee to doctrines of that country in the matter of treatment and management of syphilis.

The same objection to an even greater degree holds against the use of "Acetylarsan", which is given intramuscularly. Given by this route, the drug is slowly absorbed and never achieves anything like the concentration in the blood-stream that is brought about by intermittent intravenous injections. I suggest that this allows the development of arsenic resistance in a larger proportion of the treponema population. Besides, "Acetylarsan" is a pentavalent arsenical preparation. It has been shown elsewhere that pentavalent drugs are less efficient than the trivalent drugs in the treatment of syphilis.

Yet another factor has come into action since about 1945. The wonder drug, penicillin, so magnificent in its effect upon various coccal bacteria (staphylococci, streptococci, gonococci, pneumococci and meningococci), has been found to have a beneficial action on syphilis. But the treponema is only very distantly related to the coccal organisms and, I suggest, it is very unlikely that the effects of penicillin upon treponemata will, either in immediate or in permanent action, even approximate to its effect upon coccal organisms. Yet the triumphs of this drug in the most acute and hitherto often unmanageable manifestations of coccal diseases have established it in the minds of many as a cure-all, and I know that it is frequently used as the first and even as the only drug in the treatment of recently acquired syphilis. Many, if not most, of the practitioners who have adopted peni-

cillin as the drug of choice in the treatment of syphilis, have never seen the even more dramatic subsidence of early syphilitic lesions after the first injection of arsphenamine or neoarsphenamine. They have probably never had any first-hand experience in the treatment of syphilis, because in their student days and early professional days there were so few cases to be seen. They do not know and cannot appreciate the tenacity and capacity of survival in spite of treatment that the treponema possesses once it is established in the human body. I do not doubt that the effects of penicillin on the lesions of florid syphilis are remarkable, but I doubt if its effects are as startling to the observer as those of a full dose of neoarsphenamine in a parallel case. If it is used in the modern slowly absorbed forms, the objection applied to intramuscular injections of the arsenical drugs holds against penicillin.

Finally, the proper management of a case of syphilis requires the experience of a practised specialist, and few men in general practice can have that experience. I know, of old, that men in general practice very rarely liked to undertake intravenous injections.

When syphilis was more common, I used to undertake in private cases the intravenous injections and general management of the case (courses of treatment, dates of serum testing *et cetera*) and leave all the intramuscular injections to the general practitioner who referred the patient. This was a very satisfactory arrangement for both medical parties and for the patient. Therefore, I would urge the reinstitution of such a regime in these modern days.

The most successful routine procedure in the treatment of syphilis is recorded in my book (Molesworth, 1944). To this might be added a course or two of intramuscular injections of penicillin, but I urge that the intensive but intermittent administration of neoarsphenamine by the intravenous route should constitute the first two courses of treatment in cases of recent infection, and that the standards of cure laid down in that work should be followed exactly.

It is not reasonable to ascribe to penicillin the magic of a cure-all, and syphilis is too tenacious and too dangerous to be left to the judgement of a practitioner who has little theoretical and less practical experience of this disease.

In addition, various arsenical drugs to be taken by mouth, such as "Stovarsol" and "Spirocid", are being used in the treatment of syphilis. It must be pointed out that oral administration has been found greatly inferior to intramuscular and intravenous methods.

Dr. Cooper Booth informs me that, owing to the use of penicillin, the incidence of gonorrhœa has dropped enormously, but this is not a recommendation for the use of the same drug in the treatment of syphilis, which is due to infection with an organism widely dissimilar in nature from the gonococcus.

I feel convinced that penicillin should be used only as an adjuvant and should never be used to the exclusion of intravenous injection of neoarsphenamine, especially in the first six months of treatment in an early case of syphilis.

I wish it to be understood quite clearly that I have always been and still am definitely on the side of experimentation, but I wish to draw attention to the fact that experiments made since 1939 are now obviously failures by reason of the recent continuing increase in the incidence of syphilis, in spite of the hyperintensive use of "Mapharsen" and allied drugs given at very frequent intervals by the intravenous route, and the administration of "Acetylarsan" and similar pentavalent arsenical compounds by the intramuscular route.

This failure, I think, must be admitted, unless some cause other than that I have suggested can be suggested and supported by strong evidence. Unless such evidence can be produced, then let us return to the drugs and methods of administration which did succeed in reducing the incidence of syphilis from the 10% found by the British Royal Commission in 1910 almost to vanishing point in 1926-1942, at any rate in Australia. In other words, let us withdraw from the road which is obviously leading us to destruction, to the point at which we gained our greatest victories.

This means the intravenous injection of neoarsphenamine in maximal doses (for the individual patient) at intervals of not less than a week, and the intramuscular injection of bismuth (which cannot induce arsenic resistance). The plan of this treatment is too long to be given here, but it can be seen in my book (Molesworth, 1944).

I am sure that Dr. Cooper Booth will not take it amiss if I state that, in my opinion, and in that of many others, the only excuse for using the arsenical drugs by the intramuscular route is the inability or impossibility of delivering the dose intravenously.

I sincerely hope that he and others will take my recommendations not as reactionary criticism but as the result of the long and deeply considered opinion of one well aware of all aspects of the problem and well practised in the treatment of the disease. I have had several opportunities of discussing with Dr. Cooper Booth different aspects of the incidence and treatment of syphilis. Indeed, it was he who suggested that I should write this paper I hope that he will agree that my arguments are sound, and that he will institute a movement back to safe and proven methods of treatment of syphilis and of combating the serious health problems it presents to the community. If further experimentation is required, let it start from the "safe" position and follow from that some direction different from that which is obviously leading the community to destruction.

References.

Molesworth, E. H. (1916), "The Incidence of Venereal Disease and Method of Prevention", The Medical Journal of Australia, Volume II, page 243; (1944), "An Introduction to Dermatology", Second Edition, pages 277 to 291.

Addendum.

In the July, 1949, issue of *The Urologic and Cutaneous Review* on page 430 reference is made to a paper by V. E. Floyd in *The Practitioner* of May, 1949, in which a view similar to mine is stated. It is pointed out that penicillin is unsatisfactory as a means of producing an absolute cure in syphilis. The author recommends the use of "Neoarsphenamine" in the early stages of the disease. This drug, according to the author, can be used concurrently with the penicillin treatment.

Reports of Cases.

A CASE OF ASTHMA AND EOSINOPHILIA IN AN EX-PRISONER OF WAR.

By W. B. Stafford, M.D.,
Repatriation General Hospital, Caulfield, Victoria.

From time to time, chiefly from the tropics, cases have been reported in which asthma, with or without X-ray changes in the chest, and with a high eosinophile cell count, has responded well to treatment with arsenic compounds. Some such cases are said to be due to mite infestation of the bronchial tree (Wilson, 1947), others possibly to filariasis (Hartz and Van Der Sar, 1948). The following case is considered of interest as the condition was detected and treated three years after the return of the patient from the tropics.

Clinical Report.

A male patient, aged forty years, was admitted to the Caulfield Repatriation Hospital on September 23, 1948. He stated that, in February, 1942, he had been captured by the Japanese. Between that month and December, he worked at the dusty occupation of unloading rice, dried fish, dried seaweed and other stores at the Singapore docks. During much of 1943, he worked on the Siam railway. Between April, 1944, and July, 1945, when he was in charge of a working party at a new airfield at Changi, he suffered from repeated attacks of malaria. He recalled that, on one occasion, when crawling on the ground, weak from malaria and malnutrition, he put his finger in his throat to produce vomiting, and he thought his persisting chronic cough began on that occasion. This cough was most marked in the

TABLE I.

Date.	Total White Cell Count per Cubic Millimetre.	Cell Percentages.					Eosinophile Cell Count per Cubic Millimetre.
		Neutrophile Cells.	Eosinophile Cells.	Basophile Cells.	Lymphocytes.	Monocytes.	
September 27, 1948	—	16	46	2	29	7	—
October 1, 1948	19,000	19	68	1	8	4	13,000
October 12, 1948	19,000	8	68	—	21	3	13,000
October 29, 1948	22,200	32	48	—	17	3	10,700
November 3, 1948	22,200	17	67	—	13	3	14,800
November 10, 1948	29,200	13	66	1	16	4	19,300
November 17, 1948	10,800	26	46	1	23	4	5,000
November 24, 1948	9,800	33	20	—	37	10	2,000
December 1, 1948	7,900	53	21	—	22	4	1,700
January 12, 1949	6,100	62	7	—	23	8	430

early mornings, and with it he brought up a quantity of white to colourless sputum, but never any blood.

For the last two years, he had noted intermittent wheezing, tending to be worse in summer and to begin about eight o'clock each evening, becoming worst in the early hours of the morning. The wheezing was quite audible but never severe enough to cause him to sit up and gasp for breath. Occasionally, he noticed a moderate aching pain over the left side of the chest anteriorly, lasting up to a few hours, not related to exertion, and apparently not influenced by breathing or movement.

For two years also, he had felt unduly tired and lacking in energy, and this was becoming more marked. Despite a good appetite, in the last six months, he had lost over half a stone in weight. For three months, he had had attacks of shimmering before the eyes, lasting about half an hour, and followed by headache, but no nausea or vomiting.

To summarize, this man's main presenting symptoms were chronic cough, wheezing, loss of energy and loss of weight.

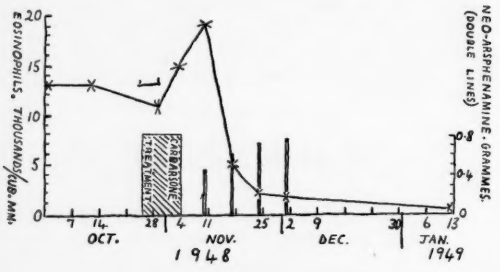

FIGURE I.

Since discharge from the army late in 1945, he had been treated for hookworm.

The patient was a thin man of average colour. His systolic arterial pressure was 125 millimetres of mercury, and his diastolic pressure 75 millimetres. Examination of his fundi and an X-ray examination of his skull failed to reveal a cause for his recent headaches. His lymph glands appeared to be normal and his spleen was not palpable. When he was first examined on September 23, 1948, his breathing was quiet, and his lungs were clinically normal. There was no tenderness to pressure about his chest, but some pain was produced over the left side of it with left lateral spinal flexion, and, to a lesser extent, with spinal rotation.

About nine o'clock one night several weeks later, low-pitched rhonchi were heard throughout the chest during deep breathing. A chest X-ray film was normal in appearance.

On October 1, the patient was found to have 12 grammes of hæmoglobin per 100 millilitres, and 4,200,000 red cells per cubic millimetre of blood. A differential white cell count on September 27 yielded the surprising figure of 46% of eosinophile cells. The total and differential white cell counts on this and subsequent occasions are shown in Table I, and the total eosinophile cell counts in Table I and Figure I.

The result of a sternal marrow count made on October 5 is shown in Table II. The pathologist commented that there was a high eosinophile cell percentage and a slightly raised myeloid-erythroid rate, but it was not considered indicative of leuchæmia.

In view of a history of hookworm, a careful search of seven specimens of fæces was made, but neither hookworm ova nor amœbæ were detected. The result of a Casoni test was negative, and mites could not be found either in a thirty-six-hour specimen of sputum or in a later twenty-four-hour specimen.

Between October 25 and November 4, 1948, the patient was given "Carbarsone", 0·25 gramme twice daily by mouth. Soon after, he stated he felt much less tired, although some wheezing persisted, but, a week later, the eosinophile cell count had risen rather than fallen. Neoarsphenamine was then given intravenously as shown in Table III. During the week after the second injection, the patient stated that he felt "splendid".

TABLE II.

Result of Sternal Puncture on October 5, 1948.

Type of Cell.	Percentage.	Type of Cell.	Percentage.
Myeloblasts	2·1	Polymorphonuclear cells:	
Premyelocytes ..	1·2	Neutrophile ..	20·0
Myelocytes:		Eosinophile ..	42·0
Neutrophile ..	0·4	Basophile	0·4
Eosinophile ..	0·9	Lymphocytes ..	14·4
Metamyelocytes:		Monocytes	2·9
Neutrophile ..	4·7	Megakaryocytes ..	0·3
Eosinophile ..	3·2	Pro-erythroblasts ..	1·5
		Normoblasts.. ..	6·0

Leuco-erythrogenic ratio: 1·7 (normal, 1·5–2·5).
Myeloid-erythroid ratio: 9·9 (normal, 2–8).

TABLE III.

Date.	Dose of Neoarsphenamine by Intravenous Injection. (Gramme.)
November 10, 1948	0·45
November 17, 1948 ..	0·60
November 24, 1948 ..	0·70
December 1, 1948	0·75

His nocturnal cough had diminished greatly, and his wheezing had disappeared, and after a further week his cough also had all but gone. When finally reviewed on January 12, 1949, the patient said that he remained very well.

The beneficial effect of treatment on the eosinophile cell count is hown in Table I and in Figure I.

Discussion.

The cause of the pronounced eosinophilia in this case was not clear. The alleged causative role of the Tyroglyphus mite in many cases of this type does not seem to have been statistically "proved" by comparison with control cases of asthma in which there was no pronounced eosinophilia.

Regardless of the cause, the important fact is that in cases of "tropical eosinophilia" the patient responds well to treatment with arsenic compounds, and the case described was no exception.

A temporary rise in the eosinophile cell count during "Carbarsone" treatment has also been reported by other observers (Apley and Grant, 1945).

It is to be noted that, though symptomatic improvement appeared to begin shortly after "Carbarsone" treatment, an initial drop in the eosinophile cell count was delayed for a few weeks, and the final normal value was not obtained until some time after completion of the neoarsphenamine injections.

Summary.

A case is reported in which asthma with a normal chest X-ray appearance and a pronounced eosinophilia occurred in a man three years after a prolonged stay in the tropics. Though no cause for the eosinophilia was found, the response to treatment with arsenic compounds, judged both by the change in symptoms and the fall in the eosinophile cell count, was quite dramatic.

Acknowledgements.

I wish to thank the Chairman of the Repatriation Commission for permission to publish this case, and also Dr. A. G. Liddelow for his repeated blood counts and sternal marrow count, and for his painstaking search of sputum for mites.

References.

Wilson, H. T. H. (1947), "Tropical Eosinophilia in East Africa", *British Medical Journal*, Volume I, page 801.

Hartz, P. H., and Van Der Sar, Ary (1948), "Eosinophilia in Filariasis: Occurrence of Radiating Processes about Microfilariæ", *American Journal of Clinical Pathology*, Volume XVIII, page 637.

Apley, J., and Grant, G. H. (1945), "Tropical Eosinophilia as Seen in England", *The Lancet*, Volume I, page 802.

Reviews.

A YEAR BOOK OF NEUROLOGY, PSYCHIATRY AND NEUROSURGERY.

A GOOD deal of specialized material is included in "The 1948 Year Book of Neurology, Psychiatry and Neurosurgery".[1] This is, of course, as it should be and will make the volume most acceptable to specialists in the several fields covered; the general practitioner and specialists in other fields will, however, find much to interest them in the wide range of literature covered. In the introduction to the first section, which deals with neurology and is edited by Hans H. Reese and Mabel G. Masten, pleas are made for a right attitude towards the results of development in nuclear physics, which have brought important possibilities of medical progress, and for a broad outlook as to his field of activity on the part of the clinical neurologist. The material in the section on neurology is grouped under headings of anatomy, physiology and pathology, convulsive disorders, electrodiagnosis, disorders of the central nervous system (cerebral trauma, cerebral infections, degenerations and intoxications, and poliomyelitis), the meninges and meningitis, cranial and peripheral nerves, nutritional disorders, disorders of the spine and spinal cord, of muscular and neuro-muscular systems, and of the vascular system, the autonomic nervous system and syphilis of the nervous system. Particular subjects are not readily singled out, but attention is drawn to the subsections on poliomyelitis and meningitis, and especially to the accompanying editorial notes, which deal respectively with bulbar involvement and the importance of initial treatment in poliomyelitis and the dangers of intrathecal therapy. Nolan D. C. Lewis has edited the section on psychiatry, which is divided into subdivisions on general topics, child psychiatry, schizophrenia, affective disorders and miscellaneous reactions, organic disorders, toxic reactions, psychoneuroses and psychosomatic disorders, and therapy. The abstracts in this section indicate the increasing amount of literature on forms of therapy, especially the so-called psychosurgery. It is reassuring to note that Lewis in his editorial notes tends to reserve judgement on psychosurgery. A more forthright attitude towards it is adopted by Percival Bailey, the editor of the section on neurosurgery. While by no means condemning psychosurgery in general, he makes caustic comment on the recently developed transorbital leucotomy (a procedure "of a nature to make a surgeon shudder" and one which "may bring a potentially useful procedure into dispute"). He draws special attention to abstracts dealing with the use of bone to repair cranial defects and has some interesting comments to make on the surgery of epilepsy, the repair of injured nerves, sympathectomy and intervertebral disk lesions. His abstracts are divided into groups on tumours, disorders of movement, epilepsy, lobotomy, infection, wounds, the vascular system, the spinal cord, intervertebral disks, peripheral cranial and sympathetic nerves, physiology and miscellaneous topics. Australian work abstracted in this volume includes a paper by V. J. McGovern and B. D. Wyke on hæmangioxanthoma of the brain, George Swinburne's study on the surgical pathology of brain abscess and a paper by H. C. Trumble on nerve anastomosis in the treatment of facial paralysis. The production of the book maintains the high standard of the series.

[1] "The 1948 Year Book of Neurology, Psychiatry and Neurosurgery"; Neurology, edited by Hans H. Reese, M.D., and Mabel G. Masten, M.D.; Psychiatry, edited by Nolan D. C. Lewis, M.D.; Neurosurgery, edited by Percival Bailey, M.D.; 1949. Chicago: The Year Book Publishers. 7" × 4¼", pp. 754, with 140 illustrations. Price: $5.00.

MINOR SURGERY.

THE second edition of "Minor Surgery" by Ogilvie and Thomson has brought up to date that convenient little book which first appeared in 1943 comprising a series of articles originally published in *The Practitioner*.[1] The need for the utmost care in dealing with minor surgical procedures is emphasized in Lord Webb-Johnson's introduction. New articles on chemotherapy and burns have been added in this edition. Soap baths might have been mentioned as a local medicament in infected burns. The excellent assortment of topics by many well-known authors has interest for every reader. Particularly must be mentioned chapters on the hand by Norman Lake, the rectum by Gabriel, and the genito-urinary system by Clifford Morson. Some orthopædists may not agree with the teaching to amputate the cocked little toe in *minimus varus*. The advice given to the surgeon who performs an occasional tonsillectomy is to select the dissection operation and leave the guillotine method to the expert guillotinist. The sound principle in treatment is stated that perianal and perirectal abscesses should be incised at the earliest possible moment. As a handbook this contribution to minor surgery has much to commend it, containing as it does a fund of helpful hints to the busy practitioner.

MUSCLES, TESTING AND FUNCTION.

HENRY O. KENDALL has been in charge of the Physiotherapy Department of The Children's Hospital School at Baltimore for over twenty-five years. "Muscles, Testing and Function" by Kendall and his wife is an admirable book giving a thorough exposition of the methods of neuro-muscular physical examination.[2]

Splendid photography enables one to see the muscles, the direction of movement and the place and direction of the examination pressure. A detailed account of the testing procedures and of the functional significance of muscle weakness and contracture is embodied in the text. The book is essentially a practical treatise.

The first chapter deals with general procedures and with the fundamental principles in manual muscle testing. The authors insist that the examiner has a great responsibility not to betray by carelessness or lack of skill the confidence that others rightly place in muscle testing procedures. Test results are useful only as they are accurate.

It is unlikely that mechanical methods will ever supplant the personal factor in muscle testing. Experience is necessary to detect the substitution movements that occur whenever spotty weakness exists. Muscle testing consists of two fundamental components: (i) test performance and (ii) evaluation of the muscle strength. The muscle testing described is directed towards examination of individual muscles in so far as is practical.

The second chapter contains thirty pages of interesting diagnostic charts for nerve lesions, poliomyelitis charts, body mechanics *et cetera*. Chapters III to VI are really an atlas of one hundred and ninety pages of illustrations and photographs in which techniques for the testing of

[1] "Minor Surgery", edited by Sir Heneage Ogilvie, K.B.E., D.M., M.Ch., F.R.C.S., and William A. R. Thomson, M.D., with an Introduction by Lord Webb-Johnson, K.C.V.O., C.B.E., D.S.O., T.D.; Second Edition; 1949. London: Eyre and Spottiswoode (Publishers), Limited. 8½" × 5½", pp. 210, with 34 illustrations. Price: 14s.

[2] "Muscles, Testing and Function", by Henry O. Kendall and Florence P. Kendall; 1949. Baltimore: The Williams and Wilkins Company. Sydney: Angus and Robertson, Limited. 11" × 8½", pp. 296, with 162 illustrations. Price: 56s. 3d.

individual muscles are clearly displayed. The authors are inclined wrongly to discount the importance of the supraspinatus muscle in the movement of abduction of the shoulder. The chapter on trunk muscles is particularly good. The authors quite rightly condemn the prevalent use of double leg raising as an abdominal exercise. An appendix which lists muscles grouped according to their joint action and their origins and insertions has been compiled mainly from "Gray's Anatomy".

A comprehensive book on muscle testing has been long overdue and this gap has now been filled. Physiotherapists, occupational therapists, physicians and orthopædic surgeons will find the book valuable in everyday practice. We commend the book to lecturers in anatomy as an aid in the teaching of medical and physiotherapy students. Whilst an intimate knowledge of the anatomical relations of muscles is necessary for surgeons, a knowledge of the function of individual muscles is more important to physiotherapists, physicians and general practitioners.

THE SZONDI TEST.

The Szondi test, which is described in a recent book by Mrs. Susan Deri,[1] is yet another test procedure which may be applied to clinical subjects in order to determine the more basic traits in their personality.

This test has been used for some years by Dr. Lipot Szondi, who had approached the subject of personality diagnosis from the viewpoint of an endocrinologist and geneticist. Szondi's theories involve an assumption that all the serious mental disorders, with the possible exception of the neuroses, are due mainly to recessive genes; he believes that when these recessive genes occur heterozygously they manifest themselves by a tendency toward the same symptomatology as is found in the main mental disorders, and that the basic psychological traits of persons will be largely determined by these tendencies.

The test consists of showing a number of pictures to the subject. The pictures are photographs of patients suffering from various types of mental disorders—homosexual, sadistic, epileptic, hysteroid, catatonic, paranoid, depressive and manic. The subject is asked to choose from amongst each set of eight pictures those which he likes and those which he dislikes. Szondi in his theory then assumes that when an affinity is shown between the subject and any particular class of disorder, as manifested in the test, then the subject possesses the recessive genes for this disorder. Mrs. Deri presents this theory in a somewhat apologetic fashion, and proceeds to show that despite the lack of external validity of the hypotheses, the test is amazingly effective in practice.

The main part of the book is a manual of the procedure of the test, and the interpretations that can be made from the results. We have as yet no samples of the test material in Australia, and so can offer no comment of a personal nature on the validity of this procedure.

The book is clear and well written, and is well worth reading for the stimulating and controversial material it contains.

MEDICINE.

In the second volume of "Medicine", Dr. Clark-Kennedy maintains the high standard set by the previous volume, "Man and Disease", and we can only echo our words of commendation of that previous volume.[2] As was then suggested, this book as a whole represents a philosophical disquisition on medicine as an art, and in no section of the two volumes is the standard other than high. The argument proceeds with continuity through the entire work, in lucid logical phrases. The whole, therefore, will be of interest to anyone connected with the practice of medicine, and will be read with delight by many not actively so engaged. We feel certain that this book will be read through, initially, by everyone, and that later it will become, as it were, a bedside book, in which doctors and undergraduates will be able to browse with increasing pleasure.

This second volume traverses successively a chapter on clinical diagnosis and one on required special investigations. This latter chapter is not without due warnings concerning unnecessary investigations, nor without ample explanation that many investigations considered necessary will prove fruitless in providing added information. The perspective provided by this chapter will be of great value. The following sections deal with disturbances of function and reactions of the mind, the latter being expressed so clearly that it is the more welcome by comparison with other abstruse dissertations on this subject. An account of pathological processes follows, and the book ends with a chapter on the practice of medicine. In this the difficulties of the seven ages of man are reviewed and the intrusion of the all-powerful State into medicine is described. At the present time this particular section appears to be most apposite.

There will be some amongst those academically inclined who will cast this book aside. It contains no straightforward descriptions of entire diseases, nor are lists of symptoms and signs to be found between the four covers. Those with their medical minds equipped as a neatly pigeonholed desk of diseases may be disappointed. The persons seeking these annotated facts must seek them elsewhere. These books will more please those who are interested in the abstract in medicine, namely, those who are interested in the practice of medicine as an art. We recommend that the disgruntled endeavour to overcome their distaste and disappointment at not finding the usual contents of a text-book of general medicine. Perseverance into this sunny philosophy of medical practice will not fail to interest them before they have read many pages.

It would be sheer pedantry to comment on the small list of points mentioned in these books on which there is no general agreement. Rather is it better to congratulate the author on the work as a whole, and to state that most of the subjects mentioned have been brought so up to date that the few errors can well be overlooked.

We have no hesitation in commending this volume to all readers, and in stating that the second volume more than fulfils the eager anticipation expressed by the reviewer of the first.

Books Received.

[The mention of a book in this column does not imply that no review will appear in a subsequent issue.]

"Training for Childbirth: From the Mother's Point of View", by Minnie Randell, O.B.E., S.R.N., S.C.M., T.M.M.G., F.C.S.P. (Hon.); Fourth Edition; 1949. London: J. and A. Churchill, Limited. 8¼" × 6", pp. 152, with 132 illustrations. Price: 10s. 6d.

Describes exercises to be carried out by the pregnant woman.

"The Principles of Chiropody", by John H. Hanby, F.Ch.S., and H. E. Walker, F.Ch.S., with a foreword by Norman C. Lake, M.D., M.S., D.Sc. (London), F.R.C.S. (England); 1949. London: Baillière, Tindall and Cox. 8½" × 5¾", pp. 396, with 129 illustrations. Price: 21s.

An attempt to provide a clear account of the background upon which chiropody is based.

"Diagnostic Tests for Infants and Children: Principles, Clinical and Laboratory Procedures, Interpretation", by H. Behrendt, M.D.; 1949. London: Interscience Publishers, Limited. New York: Interscience Publishers, Incorporated. 9" × 6", pp. 546. Price: $7.50.

Deals with "clinical and laboratory tests as used in infants and children".

"Everyday Sex Problems", by Norman Haire, Ch.M., M.B.; 1948. London: Frederick Muller, Limited. 7¼" × 5", pp. 268. Price: 10s. 6d.

A reprinting of articles published by the author in the magazine *Woman*, under the pseudonym "Dr. Wykeham Terris".

"The Rhesus Factor", by G. Fulton Roberts, M.A., M.B. (Cantab.); Second Edition; 1949. London: William Heinemann (Medical Books), Limited. 7¼" × 5", pp. 72. Price: 3s. 6d.

An account of the Rhesus factor and the part it plays in clinical medicine.

"Le sexe rôle de l'hérédité et des hormones dans sa réalisation", by Vera Dantchakoff; 1949. Paris: Presses universitaires de France. 7¼" × 4¾", pp. 218, with many illustrations. Price: fr. 480.

Deals with the factors determining sex in man and animals.

[1] "Introduction to the Szondi Test: Theory and Practice", by Susan Deri, with a foreword by Dr. Lipot Szondi; 1949. New York: Grune and Stratton. 8¼" × 5¼", pp. 372. Price: $5.00.

[2] "Medicine", by A. E. Clark-Kennedy, M.D., F.R.C.P.; Volume II: Diagnosis, Prevention and Treatment; 1949. Edinburgh: E. and S. Livingstone, Limited. 9¼" × 6¾", pp. 527. Price: 25s.

The Medical Journal of Australia

SATURDAY, OCTOBER 1, 1949.

All articles submitted for publication in this journal should be typed with double or treble spacing. Carbon copies should not be sent. Authors are requested to avoid the use of abbreviations and not to underline either words or phrases.

References to articles and books should be carefully checked. In a reference the following information should be given without abbreviation: surname of author, initials of author, year, full title of article, name of journal without abbreviation, volume, number of first page of the article. If a reference is made to an abstract of a paper, the name of the original journal, together with that of the journal in which the abstract has appeared, should be given with full date in each instance.

Authors who are not accustomed to preparing drawings or photographic prints for reproduction are invited to seek the advice of the Editor.

THE ADRENO-CORTICAL HORMONE IN RHEUMATOID ARTHRITIS.

So far only short accounts have been available in this country of the recent reports in America of the effect of the administration of what is known as "compound E" to patients suffering from rheumatoid arthritis. The preliminary report by P. S. Hench, E. C. Kendall, C. H. Slocumb and H. F. Polley, which was published in *Proceedings of the Staff Meetings of the Mayo Clinic*, has been reprinted in *Annals of the Rheumatic Diseases* of June, 1949, under the title "The Effect of a Hormone of the Adrenal Cortex (17-Hydroxy-11-Dehydrocorticosterone: Compound E) and of Pituitary Adrenocorticotrophic Hormone on Rheumatoid Arthritis". That readers of this journal may have a correct idea of this work it has seemed advisable to prepare a short summary of the report. It deals with the administration of the hormone (it is referred to as compound E) to fourteen patients who suffered from severe or moderately severe rheumatoid arthritis. In each instance the clinical features of the condition became less pronounced and the blood sedimentation rate became reduced, but when administration of the hormone was stopped a relapse generally occurred at once. Similar results were obtained with two patients who received pituitary adrenocorticotrophic hormone. In view of the scarcity of these substances and the limited data available, the report is presented as a study of certain physiological effects produced by these hormones rather than as a clinico-therapeutic report. This is a correct attitude for an investigator to adopt, but the general public and indeed the practising members of the medical profession may be forgiven if, in their anxiety to witness the relief of suffering and deformity, they look beyond the present, as they are probably justified in doing, to the time when a rich therapeutic harvest will possibly be reaped.

The work preceding the investigations dealt with in the report is of considerable interest. Since 1929 Hench has studied the beneficial effects of pregnancy and jaundice on rheumatoid arthritis. From these studies the conclusion was reached that even though the pathological anatomy of rheumatoid arthritis is more or less irreversible, the pathological physiology of the disease is potentially and sometimes dramatically reversible. "Within every rheumatoid patient corrective forces lie dormant, awaiting proper stimulation." The inherent reversibility of rheumatoid arthritis is activated more effectively by the intercurrence of jaundice or pregnancy than by any other condition or agent thus far known. Rheumatoid arthritis can be profoundly influenced by biochemical phenomena in spite of the supposed validity of the microbic theory of its origin. As time went on it became easier for Hench to look on rheumatoid arthritis as some basic biochemical disturbance which is transiently corrected by some incidental biological change common to a number of unrelated events. It seemed logical to suppose that what caused relief to rheumatoid arthritis in pregnancy was closely related to, if not identical with, the substance which gives relief to sufferers from the same disease in jaundice. Thus it was believed that the discovery of some biochemical denominator common to various agents or states beneficial in rheumatoid arthritis, but common especially to jaundice and pregnancy, would provide an improved treatment or control of the disease. The final conjecture was made that the hypothetical common denominator (or "anti-rheumatic substance X") was not a disintegration product from a damaged liver, but was a biological compound specific in nature and function, a compound which was normal to the human organism. The trouble was to find this compound. Many agents and procedures were investigated empirically and eventually it was thought that the unknown substance might be an adrenal hormone. This conjecture was strengthened by the knowledge that temporary remissions of rheumatoid arthritis are often induced by procedures known to be capable of stimulating the adrenal cortex, procedures such as the induction of anæsthesia or surgical operation. In January, 1941, Hench and his co-workers recorded their interest in adrenal cortical fractions in general and in Kendall's compound E in particular. Compound E was not available to them until September, 1948.

All the fourteen patients already mentioned suffered from "moderately severe" or "severe" chronic poly-articular rheumatoid arthritis of four and a half months' to five years' duration, which had not responded to previous therapy. The patients whose disease was of relatively short duration were already much disabled by rapidly progressive arthritis. To provide adequate controls the injection of compound E was in some cases preceded and in other cases replaced by the injection of a fine aqueous suspension of cholesterol indistinguishable in appearance from compound E. Neither the patient nor the three clinicians among the authors of this report knew when the cholesterol was substituted for the adrenal hormone. At first compound E was used, but latterly compound E acetate, which is less expensive and more easily prepared than the original compound, has been employed. The minimal daily dose required is 75 to 100 milligrammes. The initial effects on muscles and joints are described. Within a few days there occurred considerable reduction of stiffness of muscles and joints, lessening of tenderness and of articular aching or pain on motion, and significant improvement of articular and muscular function. There was a pattern in the appearance of the changes for the better and improvement often began

to appear within forty-eight hours of the administration of the hormone. Those who had found the following manœuvres difficult or impossible often were able within a few days to do them much more easily or even "normally": getting in or out of bed unassisted, rising from chairs or toilets, shaving, washing the hair or back of the neck, opening doors with one hand, wringing a wash cloth, lifting a cup or book with one hand, and climbing stairs. Other clinical effects included improvement of appetite, gain in weight and euphoria. Nine of the fourteen patients received compound E only for periods varying from eighty to sixty-one days. The compound E was then replaced by cholesterol. In eight of the nine cases symptoms began to reappear or to increase promptly and the arthritis returned. One woman patient maintained her improvement for eight weeks after the administration of the hormone was stopped. Two patients who manifested satisfactory improvement during eleven and eight weeks of injections relapsed promptly but partially when cholesterol replaced the hormone, but improved again strikingly when administration of the hormone was resumed. In one case which is reported in detail prolonged use of the hormone induced a temporary endocrine disturbance which was being studied in a metabolic unit. The important statement is made that much more experience is needed before it will be known how effective or safe the prolonged administration of compound E will be. Two female patients received pituitary adrenocorticotrophic hormone intramuscularly for twelve days and manifested clinical improvement essentially similar to that shown by those who received compound E.

No medical practitioner will read the report of Hench and his fellow workers without being thrilled by what he reads. He will think that here at last a remedy for one of man's most distressing ailments is likely to be found. This rejoicing must be tempered with caution. Hench and his fellows, as already stated, stress the view that much more experience is needed before it will be known how effective or safe the prolonged administration of compound E will be. The one patient in the fourteen who spent some weeks in comfort after the suspension of treatment with compound E, and the one who manifested an endocrine disturbance, are reminders of the complexity of the subject. On the present evidence Hench and his three collaborators appear to be justified in the suggestion that rheumatoid arthritis is basically a biochemical disturbance. This does not mean that a microbic element is not a superadded ætiological factor. It is most unfortunate, as Hench and his co-workers tell us, that supplies of compound E will not be available until 1950 and that even then supplies will be only small. The report that *Strophanthus sarmentosus*, a plant grown in parts of Africa, produces a substance which may take the place of the animal product, compound E, is encouraging. Authoritative reports on its potentialities will be anxiously awaited. Light may be thrown on the subject by investigations with compound E in other fields. For example, G. A. Perera, K. L. Pines, H. B. Hamilton and K. Vislocky report in *The American Journal of Medicine* for July, 1949, a clinical and metabolic study with compound E in hypertension, Addison's disease and *diabetes mellitus*. No useful purpose would be served by recounting in this place the details of their observations. It is not unlikely, however, that if work of a similar kind is carried on by other observers in other fields, the solution of the problem of rheumatoid arthritis will be brought nearer, and the role of compound E in its treatment defined.

Current Comment.

NOCTURNAL SECRETION IN GASTRIC ULCER.

SOME of the earlier régimes recommended for the treatment of gastric ulcer were very strict, and left the patient alone only for inconsiderable periods. Even now the alkaline powder often has a place of honour on the bedside table. If we leave on one side the ulcer of acute onset and the acute exacerbation, it is surely useful to know what happens to the gastric secretion during the hours of night. Studies of the nocturnal gastric secretion of normal persons, and those with gastric or duodenal ulcers and gastric carcinoma have been made in the Department of Medicine in the University of Chicago, and additional work has now been published by Erwin Levin, Joseph B. Kirsner and Walter L. Palmer.[1] These authors are chiefly concerned in this paper with patients who have been proved to suffer from benign gastric ulcer. Twenty-five patients have been studied, and fifty-seven separate observations carried out. Proof of the condition was obtained by the clinical course, by radiological examination and gastroscopy, or by a combination of these methods. In every instance the patient had abdominal distress of the characteristic kind, and an ulcer crater was demonstrated by X-ray examination. The volume and acidity of the nocturnally secreted gastric juice were determined, and the output of free hydrochloric acid. Multiple tests showed that a patient secreting a small amount of acid on one night would repeat this type of secretion on a succeeding night; the same was true also of those whose secretion was highly acid. Hourly variation was found to be very slight, it was rare to find a lack of secretion for an hour, and in no instance was there an absence of secretion for as long as two hours. The average secretion tended to diminish gradually until 5.30 a.m., after which there was a gradual increase. The lowest output was between 3.30 and 5.30 a.m., that period which seems to be slack tide in most human beings. Considerable variability was observed in the rate of secretion, which often fluctuated from hour to hour. But although the general average stability of gastric secretion was a feature in most of the subjects, the amount of free acid produced varied considerably. Only in four-fifths of the studies carried out did the secretion of acid persist throughout the night. In 76% acid was absent for as long as two hours or longer, and in 13% no acid was produced during the night hours. There was no constancy in the period during which the greatest amount of acid was secreted. This is an interesting observation, that although the secretion of gastric juice is steady through the night, that of hydrochloric acid is discontinuous. When these patients were compared with normal persons and with those suffering from duodenal ulcer it was found that those with duodenal ulcer secreted a greater concentration, volume and output of acid than those with benign gastric ulcer. The latter secreted an average volume of gastric juice which did not differ significantly from that of normal individuals during the night, but the concentration of free hydrochloric acid and the output of acid were actually lower in the patients with benign gastric ulcer. The authors point out that variations in different patients make it difficult to construct composite curves of the rates of secretion, but their observations have been made on sufficient clinical material to enable them to make these generalizations. The most surprising result is the finding that the concentration of free acid and the volume of total acid are lower in patients with gastric ulcer than in those with duodenal ulcer and also in normal subjects. There was no consistent coordination found between the gastroscopic findings and the amount of acid excreted, though secretion was lower in

[1] *Annals of Internal Medicine*, May, 1949.

persons with an associated atrophic gastritis. No explanation is given for the differences between the three groups investigated. It cannot be said that the riddle of the peptic ulcer is yet solved, even from the biochemical point of view. Perhaps this is to be expected, as it is certainly a subject which demands study from every relevant angle.

PROPHYLACTIC SULPHANILAMIDE THERAPY IN RHEUMATIC FEVER.

FROM time to time in these columns we have reviewed current work and opinions on the use of sulphonamide drugs as a prophylactic measure against recurrence of rheumatic fever. In a leading article on May 8, 1943, a survey was made of important literature of the time and it was found that sulphonamide prophylaxis stood generally in a favourable light. Since then conflicting and, to the general medical reader, perplexing views have been expressed. In a symposium published in *The American Journal of Medicine*, to which we drew attention on July 19, 1947, the prophylactic value of sulphonamides was upheld by H. F. Swift, but treated with great reserve by M. G. Wilson. Wilson considered the approach valid, but stated that published studies did not meet the basic requirements for adequate biostatistical analysis and that final judgement as to the validity of the ætiological concept and consequent preventive therapy which were based on those studies must be deferred. An investigation of impressive size and scope has now appeared, and it is claimed that the material presented fulfils the criteria which Wilson considered essential for an adequate biostatistical analysis. The paper is of particular interest in that the work is Australian, being reported by S. D. Rubbo, M. C. Holmes and H. L. Stokes, of Melbourne.[1] It represents the result of investigations carried out at the Children's Hospital, Melbourne, since 1944. Small daily doses of sulphanilamide have been given to 211 children aged from four to fourteen years for 565 person-years, and over the same period 337 children have been observed as controls for 971 person-years. The two groups were closely matched, particular attention being paid to (i) age distribution, (ii) time of start of prophylaxis in relation to a major episode, (iii) severity of initial attack, and (iv) susceptibility towards recurrence due to environmental factors. A recurrence of rheumatic fever was diagnosed on the appearance of one or more major manifestations—polyarthritis, carditis and chorea—necessitating complete rest in bed and admission to hospital. The expected recurrence rate for children aged four to fourteen years, as established from the control group, was 11·8%; the rate amongst those receiving prophylactic therapy was 3·2%. These figures are stated to be statistically significant and so add considerable weight to earlier claims that continuous prophylactic administration of sulphonamide in doses of the order of one gramme a day to ambulant patients who have had one or more attacks of rheumatic fever will significantly reduce the risk of further occurrence. Investigation of the hæmolytic streptococcal carrier rate in the two groups of patients revealed a significant reduction in the incidence of group A in the treated group. Sulphanilamide-resistance tests carried out on 669 strains isolated from both groups of patients revealed that 29% of group A strains isolated from the treated group and 6% from the controls were resistant to 10 milligrammes of sulphanilamide per 100 millilitres. However, it is not considered that the fact that sulphonamide-resistant organisms are developed is sufficient ground for the discontinuance of prophylaxis, and Rubbo and his colleagues present ingenious arguments which suggest that the development of resistance is not as serious as might be made out. The other objection usually raised to continuous sulphonamide prophylaxis—the toxic effect of the drug—is similarly minimized. Careful observation of their patients—and it must be conceded that the scope of the observation was considerable—has failed to reveal any major toxic reactions and very few minor effects. However, they do not recommend the medication unless patients can be observed at regular intervals and appropriate laboratory examinations can be made. Subject to that qualification they consider that all patients who have had undoubted rheumatic fever or chorea should, if circumstances permit, be given the benefit of the treatment; it is important for those with the disease in a mild form as well as for those who have it in its severer forms. The treatment should begin in a quiescent period after a major episode and should be continued at least during the years of susceptibility to recurrence, that is, up to the age of fourteen years. These claims and recommendations are in line with those of the early enthusiasts and, based as they are on prolonged observation of a large series of patients, they go far to counter the more recent swing to a cautious and even disparaging view of sulphonamide prophylaxis.

[1] *The Lancet*, August 20, 1949.

NORMAL IRON RESERVES.

THE iron reserve of the body is an important limiting factor in hæmoglobin regeneration. If it has been depleted or is inadequate to meet the demands of repeated blood loss, for example, blood donations or menstrual loss, the individual becomes dependent upon his day-to-day dietary intake of iron, which then requires careful examination for adequacy. Martin Hynes[1] has pointed out that no one seems to have attempted to measure the reserve of iron available for hæmoglobin synthesis in man, though it has been estimated that in a dog 57% of the total iron was contained in the blood hæmoglobin, 20% was stored in a form potentially available for hæmoglobin synthesis, and 23% was bound in myohæmoglobin, cell enzymes *et cetera*, and was not available for hæmoglobin formation. The available iron reserve of the dog was thus sufficient to replace about one-third of its circulating hæmoglobin. Martin set out to calculate the iron reserve in man, working on the basic assumption that if a man is kept anæmic by repeated bleeding, his rate of hæmoglobin regeneration will fall progressively until, when his iron reserve is exhausted, he will be entirely dependent upon dietary iron intake and a constant level of hæmoglobin regeneration will be attained. The subject of the experiment was a normal man, aged thirty-seven years, weighing 63 kilograms, who had lived on the normal English civilian diet since his discharge from the army sixteen months before the experiment began. It is not necessary to describe here the details of method and calculation, but the iron reserve was calculated by Martin to be about 600 milligrammes, sufficient to replace about one-fifth of the subject's red cells. As Martin states, the relative smallness of this reserve emphasizes the importance of iron therapy after any substantial hæmorrhage. It was further calculated that the present English diet can yield four milligrammes of iron daily for hæmoglobin synthesis in addition to the normal needs for replacing effete red cells; this extra four milligrammes would replace a loss of only eight millilitres of blood a day. The body must depend almost entirely on its available iron reserve for rapid recovery from hæmorrhage, for the dietary iron suffices for a hæmoglobin increase of only 0·15 gramme per 100 millilitres per week. The relationship of these findings to blood loss by donation and by menstruation is of interest. Martin states that the iron reserve would not be depleted by blood donations of 450 millilitres as often as five times a year by a man or by a woman with normal menstrual loss. Moderate menorrhagia, however, could of itself demand more than the available four milligrammes of extra iron. These are, of course, British figures, relating to a fairly constant rationed intake with decided limitations. It would be of interest to know the position in this country. The dietary intake would be much more variable, but probably higher on the average. The relationship of the findings to the interval between blood donations is still of practical importance.

[1] *Journal of Clinical Pathology*, May, 1949.

Abstracts from Medical Literature.

MEDICINE.

The "Rice Diet" for High Blood Pressure.

H. A. Schroeder *et alii* (*Annals of Internal Medicine*, April, 1949) found that the "rice diet" (unsalted rice, fruit juices and vitamins) reduced the diastolic blood pressure in a minority of patients who took it and that the changes were not striking. When the disease process was advanced, neither salt restriction nor the rice diet appeared to be efficacious.

Dorothea G. Loofbourow *et alii* (*The New England Journal of Medicine*, June 9, 1949) found that a significant fall in blood pressure occurred in six out of sixteen patients who adhered strictly to the rice diet and in three out of twenty who adhered "moderately" to it. The authors class as strict adherers all patients whose urinary chloride excretion falls to ten milliequivalents per litre or less; those with chloride excretions between ten and fifty milliequivalents per litre are called moderate adherers, and those with greater chloride excretions are called delinquents.

Streptomycin in Tuberculosis.

K. H. Pfuetze and M. M. Pyle (*The Journal of the American Medical Association*, March 5, 1949) discuss the treatment of tuberculosis with streptomycin in America over the last three years. They state that in disseminated tuberculosis and tuberculous meningitis treatment is indicated at once. Cutaneous sinuses and associated lymphadenitis heal well, and tuberculous bones and joints and pleural and anal fistulæ derive benefit from streptomycin; ulcers of the mouth, pharynx, larynx and trachea respond well, as do tuberculous enteritis and peritonitis. Genito-urinary tuberculosis has been alleviated, or apparently cured in a large number of cases. *Otitis media*, pericarditis and ocular tuberculosis respond fairly well. Brain lesions do not respond, because streptomycin does not penetrate the brain. Tuberculous pleurisy with effusion tends to regress spontaneously, yet a course of two or three weeks of streptomycin is advised in this disorder. Empyema does not respond to streptomycin, although the drug penetrates into the pleural cavity quite well when given intramuscularly. In pulmonary tuberculosis great care is needed. The best results occur in recent exudative lesions, but it is advisable not to use streptomycin if the patient is likely to recover without it, because of the danger that the bacillus may become resistant to streptomycin after one course of treatment. In such a case, if the disease persists, as it often does, streptomycin will have lost its value, and the outlook may be worse than ever. Streptomycin should not be used prophylactically, but only when a definite lesion has arisen. Streptomycin is only one factor in the treatment of tuberculosis, and all other methods of treatment must be employed. Intramuscular injection of 0·5 to 1·0 gramme per day is the usual method of treatment, but for meningitis intrathecal as well as intramuscular injection is necessary. Resistance of tubercle bacilli usually develops in a few weeks, so that streptomycin treatment should be limited to five or six weeks or less. Intermittent administration, by giving two grammes of streptomycin for one day in five for one hundred and twenty days, appeared in a few cases to be less productive of resistance in the organisms. The use of "Promin" also in conjunction with streptomycin in tuberculous meningitis appeared to reduce the resistance of organisms to streptomycin treatment. The toxicity of the drug is less with the smaller doses, though nausea, fever, skin rashes, pruritus, exfoliative dermatitis, granulocytopenia and aplastic anæmia have been reported. In pregnancy streptomycin has been used successfully.

Primary Atypical Pneumonia.

E. B. Schoenbach and M. S. Bryer (*The Journal of the American Medical Association*, January 29, 1949) discuss treatment of primary atypical pneumonia (non-bacterial) with aureomycin. The authors, in describing the condition, refer to the gradual onset, the few signs, the low leucocyte count, the lack of response to sulphadiazine and penicillin, and the appearance of cold agglutinins in the serum of patients for human group O cells, or agglutinins for *Streptococcus MG* during the course or convalescence. Negative results of tests for viruses and rickettsias were recorded, and the authors state that pneumococci or other pathogenic organisms were frequently not isolated from sputum, nose or throat. Nevertheless various organisms were recovered from nose and throat and sputum, and the main criterion of diagnosis seems to have been the failure to respond to sulphadiazine or penicillin. Thirteen of the patients were treated with aureomycin given orally, 100 to 250 milligrammes hourly for three doses and the same dose every two hours till fever subsided, then 15 to 20 milligrammes per kilogram every four to six hours for two to five days. The response to this treatment was good, and the authors recommend it when other conditions can be excluded as the cause of the pneumonia.

Massive Hæmatemesis.

C. Costello (*Annals of Surgery*, March, 1949) states that an analysis of 300 cases of massive hæmatemesis showed that the ætiology was in 57% of cases chronic duodenal ulcer, in 14% acute gastritis, in 11% chronic gastric ulcer, in 8% ruptured œsophageal varices, in 4% chronic gastritis, in 1·3% gastric carcinoma, in 1·3% stomal ulcer, in 0·6% Curling's ulcer and in 1·0% carcinoma of the œsophagus. In 82% of the cases the patients were male and the highest incidence was in the sixth decade. The over-all mortality was 25%. The mortality rate varied with the age of the patient; in the fourth decade it was 10%, in the fifth 20% and in the seventh 38%. It varied also with the cause of the hæmorrhage, being highest with carcinoma of the stomach and least (9%) with chronic gastritis. At post-mortem examination many of the eroded vessels contained antemortem clot. Thus death was not from continued hæmorrhage, but from the complications of diminished blood volume. The practice of waiting for a fall in blood pressure to 80 or 100 millimetres of mercury before administering a "small transfusion" is a direct contradiction of sound physiological principles. With an adequate blood replacement plan, 4% of 73 patients died compared with 25% of the 300 treated by various methods. The author considers that the use of intravenous saline therapy is to be condemned, as not only does it not improve the blood volume, but it encourages the development of pulmonary œdema. The time factor is important in the blood-replacement therapy. A bedside estimation of the blood changes by the copper sulphate method is used. Early and enthusiastic diagnostic steps were found to be harmful, as was the practice of gastric siphonage or lavage. Two hundred millilitres of a predigested protein-carbohydrate-vitamin mixture were given every two hours. The patient was kept drowsy by the initial use of morphine sulphate followed by hypodermic injections of sodium phenobarbitone. The use of surgery in the acute phase was not recommended. The results did not compare with active non-operative treatment.

Venous Congestion of the Heart.

L. Unghvary (*American Heart Journal*, April 1, 1949) has produced venous congestion of the heart in dogs by the application of ligatures to the coronary sinus. Characteristic abnormalities of the electrocardiogram developed, the most striking and consistent change being a reduction of the amplitude of the *R* waves, with or without the appearance of a deep *S* wave. In most cases the *T* wave became smaller; sometimes it became inverted.

Treatment of Hyperthyreoidism in Children.

John H. Lyons (*Annals of Surgery*, May, 1949) discusses the treatment of hyperthyreoidism in children. He states that the condition is rare in children, particularly in the very young, and is especially rare in male children. The ætiology is vague, but heredity, infectious disease and psychic trauma have been considered important factors. No case of adenomatous goitre with hyperthyreoidism has been seen at the Mayo Clinic; the gland is moderately and rather symmetrically enlarged and is usually firm in consistency throughout its entire substance. The symptoms of the condition in children are analogous to those in adults with exophthalmic goitre. Tachycardia, exophthaimos, goitre and tremor are almost constantly present. Increased appetite, heat intolerance, sweating, increased pulse pressure, weakness, loss of weight, dyspnœa and gastro-intestinal disturbance may be present. Although the disease may be severe in children, crises are not common and the course is characterized by periods of remission and exacerbation. Early diagnosis is of importance, but diagnosis is rarely made early. The determination of the basal metabolic rate is of questionable value in a nervous and often non-cooperative child. In the past subtotal thyreoidectomy has been the recommended treatment after preparation of the patient with iodine. The hope of pædiatricians that thiouracil or the safer propyl thiouracil would prove a substitute for surgery has not been realized. Treatment by irradiation or the more recent therapeutic agent radioactive iodine is condemned. The author concludes that iodine is the drug of choice in preparing children for operation and that subtotal

thyreoidectomy remains the best treatment for hyperthyreoidism in children. Propyl thiouracil is used only as a preparation drug in those cases in which iodine fails to reduce the basal metabolic rate and allay the symptoms so that a single-stage thyreoidectomy can be carried out safely. The reasons given by the author are, firstly, that the type of hyperthyreoidism always present in children, namely, diffuse hypertrophy, responds especially well to iodine; secondly, that the child can be much more rapidly prepared for operation with iodine than with a thiourea derivative; and, thirdly, that iodine is a safe drug, while thiouracil and even propyl thiouracil are potentially dangerous.

Antihistamine Therapy for Bee Stings.

W. T. STRAUSS (*The Journal of the American Medical Association*, June 18, 1949) discusses the stinging mechanism of the bee, the nature of bee venom and the effects produced by bee stings. He states that it is generally believed that allergy plays some role in the human response to bee stings and refers to the histamine-like action ascribed to bee venom by other investigators. He reports the effect of local application of an ointment containing an antihistamine preparation "Thephorin" in 5% strength in a series of eight cases of bee sting and other insect bites (including ant bites). The ointment was applied liberally at the site of the sting as soon as possible, usually within a few minutes after the sting occurred, and the site gently massaged to aid absorption. Relief of pain was almost immediate and swelling of the affected part rarely occurred. No side effects of any kind were observed.

Nitrogen Mustard Therapy.

C. C. SHULLENBERGER, CHARLES H. WATKINS AND ROBERT R. KIERLAND (*The Journal of the American Medical Association*, March 19, 1949) present an analysis of results of nitrogen mustard therapy, or combined nitrogen mustard and irradiation therapy, in eighteen cases of advanced Hodgkin's disease. Nitrogen mustard therapy was found to have very limited usefulness in cases in which the disease had become refractory to irradiation therapy. Lesions which involved non-lymphoid organs responded poorly or not at all to nitrogen mustard therapy. The results of nitrogen mustard treatment in ten cases of lymphosarcoma were found to be not encouraging and also to be unpredictable; some patients may respond very well. No conclusions were drawn as to the correlation between the histological pattern in a given case of lymphosarcoma and the responsiveness to therapy. The authors found nitrogen mustard a valuable adjunct to irradiation therapy in the treatment of *mycosis fungoides*, although response varied in different cases. Initial results in the treatment of *polycythæmia vera* with nitrogen mustard were sufficiently encouraging to warrant further investigation of its use in this disease. Malignant neoplasms responded very poorly or not at all to nitrogen mustard therapy. The authors point out that nitrogen mustard is potentially a dangerous drug, and is capable of severely damaging the hæmatopoietic tissues when used in the currently accepted therapeutic doses. A true evaluation of the efficacy and reliability of nitrogen mustard in cases of lymphoblastoma can be determined only by comprehensive controlled experiments.

S. BEN-ASHER (*The American Journal of the Medical Sciences*, February, 1949) reviews the results of treatment with nitrogen mustard of Hodgkin's disease, leuchæmia, lymphosarcoma and cancer of the lung. Methyl-bis(β-chloroethyl) amine hydrochloride was given intravenously in a daily dose of 0·1 milligramme per kilogram of body weight for four days, then every two to four days. It was injected either directly into the vein or into the rubber tubing during a saline infusion. Great care was taken to avoid extravasation of the solution or prolonged contact with the skin. Additional courses were given in two to sixteen weeks, depending on the progress and response. Thirteen patients with Hodgkin's disease who had previously had X-ray therapy and were resistant to treatment responded well. Remissions are said to have occurred in eleven cases, good results in six and four in five. In lymphatic and myelogenous leuchæmia and lymphosarcoma results were not so encouraging, nor was benefit observed in carcinoma of the lung. Toxic effects included nausea and vomiting, which began two to six hours after an injection and lasted three to twelve hours. Preliminary sedation relieved this. Thrombosis in the vein injected was usual, but less frequent when rubber tubing was used. In the blood reduction of the number of lymphocytes, granulocytes and platelets was observed for two or three weeks. The conclusion was that nitrogen mustard was of some value in Hodgkin's disease, but not in the other conditions.

A Diagnostic Test with B.C.G.

H. J. USTVEDT AND A. AANONSEN (*Acta tuberculosea Scandinavica*, 1949) suggest a test to make it possible to pick out from those whose reactivity to the intracutaneous tuberculin test is in doubt any who may harbour a living tuberculous infection. They make two punctures in the skin through a drop of B.C.G. vaccine containing 20 milligrammes per millilitre; the formation within six days of distinct papules indicates a specific reaction. They also suggest the employment of this test in the case of persons, vaccinated with B.C.G., who fail to react to tuberculin after vaccination.

Massive Myocardial Infarction.

ARTHUR SELZER (*Archives of Internal Medicine*, August, 1948) reports some clinical observations in 28 unselected cases of myocardial infarction, in which the pathological diagnosis of recent massive myocardial infarct was made at autopsy. The symptomatology, clinical course and laboratory and electrocardiographic findings are correlated. The author states that, in this series, the initial attack, the effects on the circulation, and the constitutional reactions of acute myocardial infarction were not of uniform severity. There was a predominance of mild and moderately severe clinical manifestations over extremely severe ones, and this suggested that there was no close relation between the clinical picture and the anatomical changes in the myocardium. In spite of severe damage to the myocardium, several patients showed no evidence of serious circulatory insufficiency, and presumably would have recovered if they had not succumbed to secondary complications, which developed in the course of acute myocardial infarction. Four lead electrocardiographic studies were not appreciably helpful in the diagnosis of massive myocardial infarction. Atypical patterns occurred in the majority of cases, and in some of them only minor deviations from normal were present. The practical significance of the findings lies in the demonstration of the fact that massive myocardial infarction may cause benign clinical symptoms, suggesting only minor damage to the myocardium, or may even make the presence of a recent infarct questionable.

Thyreotoxicosis.

WILLIAM H. BEIERWALTES AND CYRUS C. STURGIS (*The Practitioner*, June, 1949) discuss the present state of the treatment of thyreotoxicosis, and state that the administration of iodine followed by subtotal thyreoidectomy may be employed for patients with uncomplicated exophthalmic goitre who are suffering from only mild toxicity. However, a more satisfactory result is obtained by the use of propyl thiouracil *plus* iodine. The highest incidence of "cure" is achieved with propyl thiouracil and iodine alone. The optimum pre-operative treatment of patients with both nodular and non-nodular goitres of moderate to severe toxicity is 300 milligrammes of propyl thiouracil and four drops of Lugol's solution per day. This should be continued until the basal metabolic rate is at or under zero. All large exophthalmic goitres and all nodular toxic goitres should be removed surgically; propyl thiouracil with iodine may be used alone, in an attempt to produce a "cure" in cases not included in this group, and in cases with a high anticipated surgical mortality; there is an 80% chance of success in a selected group. The indications for use of radioactive iodine are those for the use of propyl thiouracil with other limitations, such as possible danger to the patient and the difficulties of securing the material and controlling its use. The authors state that the chief use of iodine today in the treatment of patients with thyreotoxicosis is in augmenting the antithyreoid effect of propyl thiouracil, and in reducing the hyperplastic changes produced by propyl thiouracil given pre-operatively.

Barraquer's Disease.

LUIS BARRAQUER FERRÉ (*The Journal of Nervous and Mental Disease*, February, 1949) has observed ten cases of progressive cephalothoracic lipodystrophy (Barraquer's disease). It is characterized by absence of fat tissue in the face, arms and trunk in contrast to a normal or increased accumulation of fat in the lower half of the body. It is said that the Pharaoh Amenonphis IV suffered from this condition. In one of the author's cases the patient had a dystrophic inheritance through three generations. In all his cases the patients were females. The author excludes a hormonal cause and considers that the condition is due to a hypothalamic heredodegeneration. The latter results in liberation of the subordinate vegetative centres, especially those of the cervical sympathetic chain. The hyperactivity induced leads to destruction of the fat.

Special Abstract.

DRUGS IN THE TREATMENT OF RHEUMATIC DISORDERS.

A CONSIDERABLE number of drugs have established their position in the treatment of rheumatic disorders, some of them for many years. The recent development of the adrenal cortical hormone compound E for the treatment of rheumatoid arthritis appears to be opening a new chapter in the story of the rheumatic group of conditions (see the leading article on page 509), but the older drugs are still important. A helpful survey and evaluation of these drugs has been recently made by N. Mutch[1] and should be of general interest. Mutch points out that drugs are important in the treatment of rheumatic disorders, but their role is essentially a contributory one, to be fitted into the general therapeutic plan. Their greatest uses are to be found in acute rheumatic fever and its clinical variants, gout, non-articular fibrositis, and those forms of chronic arthritis, typified by rheumatoid arthritis, in which intermittently progressive inflammatory lesions are produced in joints which have become subtly potentiated or in joints which have been involved during acute bacterial infections; the group includes joints in which the lesions of chronic inflammation are modified by those of coincident growth, senescence, trauma, osteoarthritis and gout.

Rheumatic Fever.

In the treatment of rheumatic fever salicylates maintain their time-honoured pride of place, though their striking clinical effects still lack pharmacological explanation. Various investigators have produced conflicting reports, but Mutch considers that the idea still remains plausible that the rapidly formed effusions of acute rheumatic fever result from the combined effects of capillary damage by histamine and the diffusion of toxins by hyaluronidase, and that salicylates give clinical relief by inhibiting the effects of the former process, the basic assumption being that rheumatic pain is caused by the local occurrence of exudates. Whilst the symptomatic value of salicylates is undisputed, it still remains uncertain how far the drugs can eradicate the disease itself or even benefit the rheumatic heart. After much research, Mutch states, their claim to act as true chemotherapeutic agents remains unproven.

Sodium Salicylate.

Sodium salicylate, the salicylate drug usually employed, when taken by mouth is quickly absorbed and attains a peak plasma concentration in two hours. Elimination is slower than absorption, and a two-hourly dosage scheme produces cumulation with a steady rise in plasma concentration; if large individual doses are repeated, toxic symptoms occur. Some salicylism always occurs before the full therapeutic effect on joints and fever has been attained. Mutch discusses the work of Coburn and others on massive salicylate therapy, and comments that the severe degree of poisoning often induced would be justified if there was full assurance that the incidence of cardiac lesions could indeed be reduced; the results of all workers have not provided this assurance. It would appear, he states, that as yet there is no proven advantage in modifying the traditional routine of allowing the relief of pain and swelling in the joints to be the criterion of adequate dosage, the patient being expected to submit to the discomforts of mild salicylism, but not to the major risks of intoxication or intolerance.

Acetylsalicylic Acid.

If sodium salicylate is not tolerated acetylsalicylic acid may be substituted. This is less toxic and has a much greater antirheumatic effect, but it may give rise to idiosyncrasy, which precludes its use, or to gastric irritation, which may be largely overcome with potassium citrate.

p-Aminobenzoic Acid.

The clinical effect of salicylates is increased by *p*-aminobenzoic acid, and in heavy dosage it has some direct influence on the joint manifestations of rheumatic fever. Its chief action is to diminish the rate of salicylate excretion by the kidneys and so raise the blood salicylate level.

Cinchophen.

The effect of cinchophen on the rheumatic fever syndrome closely parallels that of salicylates, but it may irritate the stomach and even produce angioneurotic œdema or symptoms resembling salicylism. Patients intolerant of sodium salicylate can usually take cinchophen without distress, but it should be reserved for cases of extreme salicylate idiosyncrasy, as it may, though rarely, cause a fatal form of hepatitis, the incidence of which is not determined by the magnitude of the dose, the length of the course already taken, or any previous use of the drug. Hepatitis has followed the use of the methyl ester ("Novatophan"), the allyl ester ("Atoquinol") and neo-cinchophen.

Amidopyrine.

The pain, pyrexia and joint swellings of rheumatic fever respond to amidopyrine. It does not irritate the stomach, but it may unpredictably cause fatal agranulocytosis.

Sulphonamides.

Simple sulphonamides and penicillin have both proved powerless to give symptomatic relief or check the course of rheumatic fever, but evidence has been presented that sulphonamides may diminish the relapse rate. Mutch considers that there is insufficient evidence on the point to justify the systematic dosing of patients with drugs possessing such harmful potentialities.

Gout.

As the intrinsic nature of gout is still obscure, treatment remains empirical and intuitive.

Acute Gout.

Most patients obtain dramatic relief from acute attacks of gout with colchicum, though some do not respond. It is given as colchicine 0·5 milligramme or *Vinum Colchici* one millilitre every two or three hours for four or five doses and then at longer intervals till relief is obtained or untoward symptoms occur. Opium counteracts looseness of the bowels, but should not be allowed to cause constipation. Colchicine is cumulative and very poisonous; a total intake of eight milligrammes should not be exceeded lightly. Salicylates may be used with or instead of colchicine; they lessen pain and inflammation around the joints, but benefit beyond this is disputed. Cinchophen, 0·5 milligramme every two hours for six or more doses, relieves pain.

Chronic Gout.

The drugs in widest use for chronic gout are cinchophen and salicylates, which effectively relieve the pain and increase the excretion of uric acid, lowering its titre in the blood. In the absence of disease in the liver, kidney and blood vessels, cinchophen can be taken for three or four days in each week for long periods in doses of 0·5 to 1·5 grammes daily until the concentration of urates in the blood becomes normal. Sodium bicarbonate may be given to lessen gastric irritation due to cinchophen and to supplement the citrates, acetates and bicarbonates of sodium, potassium and lithium commonly given to render the urine alkaline and keep the extra urates in solution. As an alternative generous doses of salicylates may be given with protective alkalis; to secure results of sufficient permanency the course of treatment should be kept up for three or four weeks.

The Rheumatoid Group.

Treatment methods based on modern concepts of the pathogenesis of conditions of the rheumatoid group are designed to protect the joints from noxious substances of microbic and other origins present in the blood, and to promote the healthy activity of all vital functions depressed by abnormal circumstances of the patient's habits and environment. There are also putative chemotherapeutic agents for the destruction of hypothetical causal organisms. Mutch sums up the medical measures of most proven worth in the treatment of rheumatoid arthritis and other rheumatic conditions of chronic inflammatory type in five groups: those concerned with the cleansing of areas of surface infection, the correction of alimentary aberrations, the maintenance of the efficiency of vital functions, and the relief of pain and distress, and chrysotherapy. He points out that although the primary cause of rheumatoid arthritis remains obscure, much is known about those perpetuating factors which determine the chronicity of the local inflammatory process and the rate of structural disintegration. The rheumatic joint differs from, for example, the tuberculous joint in that it appears to be much more vulnerable to abnormal blood constituents which provoke inflammatory reactions of varying intensity. What these substances are and how they act are matters for further inquiry; they are not necessarily related directly to the elusive primary cause.

[1] *Annals of the Rheumatic Diseases*, June, 1949.

Septic Foci.

The septic focus, Mutch states, has long been held to be an important generating point of these provocative substances and little success can be expected from medicinal treatment unless all surface areas of gross infection have been effectively cleansed by dental and surgical procedure. Extensive infection of a chronic type may persist in the throat, nose and sinuses after all operative measures have been taken, and Mutch recommends for these the use of nebulized mists of penicillin and sulphonamide. Hand nebulizers are inadequate; apparatus operated by oxygen pressure or by an electrically driven compressor is needed.

Alimentary Aberrations.

After surface areas of infection are dealt with, attention can be focused on the digestive tract where provocative substances might gain access to the blood from inflamed organs, from polypi or other tumours, from microbic infestation of the mucosa, and from the bowel contents themselves. It has been found that molecules of sufficient complexity to retain antigenic properties can pass through the intact lining of the bowel. The normal products of digestion appear to be innocuous, except to those subject to food allergy. The production of pathogenic compounds is due chiefly to microorganisms. All deviations of digestion should therefore be corrected and opportunities reduced for the production and absorption of antigens and other provocative compounds thrown off by the intestinal flora or arising from the action of digestive enzymes operating in a bacterially contaminated medium. The diet must be simple and correctly balanced. Evacuation must be satisfactory; colonic lavage may help the severely constipated.

Digestants.—Two digestant substances are considered to be of practical value. Takadiastase, which converts starch to sugar, aids when, with the retention of an excess of carbohydrates in the colon, the streptococcal elements in the flora gain dominance over the coliform organisms; its administration should be combined with simplification and reduction of starchy foods in the diet and treatment of constipation. Erepsin speeds the later stages of protein digestion and so reduces the amount and complexity of the protein remnants which reach infected areas of the lower part of the bowel.

Intestinal Antiseptics.—The older types of intestinal antiseptic have long been discredited. Sulphaguanidine, succinylsulphathiazole and phthalyl-sulphathiazole reduce the colonic flora, but their application is very limited; they may improve a patient's general condition, but not the state of the joints. Halogen-substituted phenols have been found useful. If taken some hours after the last meal of the day, solutions of monochlorophenols and dichlorophenols probably maintain bacteriostatic concentrations in the small intestine for a time and so protect the processes of normal enzymic digestion from chemical distortion by collateral microbic action. The diminution in rheumatic pain which can follow such medication, Mutch states, is often so striking as to suggest that some additional mechanism may be at work, such as the denaturing of abnormal breakdown products with harmful antigenic properties by their linkage with the administered drug.

Mineral Adsorbents.—If provocative substances entering or formed in the digestive tract could be destroyed, precipitated or removed from aqueous solution in some way, they would be prevented from reaching the circulation. Of mineral adsorbents given with this objective, kaolin and acid-resistant alumina have appeared clinically to give most relief in rheumatic disorders. Kaolin with a suitable aperient is given before breakfast and at bedtime. Alumina can be given as a supplement to kaolin since it adsorbs an entirely different range of compounds; it should be selected for its adsorption potency and its freedom from antacid activity.

Upper Alimentary Lubrication.—The administration before meals of a 25% to 30% oil-in-water emulsion of well-homogenized heavy mineral oil, especially if combined with an adsorbent, is said to be useful for rheumatoid patients who are confined to bed and for others with persistent simple dyspepsia.

Specifics.

Gold.—Gold, a number of organic compounds of which are available, has established its therapeutic usefulness. It has been suggested that it produces its therapeutic effects by stimulating phagocytes, but evidence is steadily accumulating in favour of the view that its action is a truly chemotherapeutic one leading more directly to the death of invading organisms. It is widely agreed that chrysotherapy is appropriate only for arthritis of chronic infective type in its active stage when the blood sedimentation rate is high. The risk of serious toxic manifestations is greatly reduced if patients with kidney, liver, skin and cardiovascular disease are excluded and the more conservative modern scales of dosage are employed, for example, intramuscular injections of sodium aurothiomalate in individual doses scaled from 0·01 to 0·05 gramme at intervals of a week and continued to a maximum total of 0·5 gramme. After a rest period of two to three months to provide opportunities for elimination the injections can be continued at similar rates, but even smaller doses have been recommended by experienced workers in this field. The response is usually either a long and steady improvement or a painful joint reaction with, perhaps, slight fever; in the latter case modification of dosage may be desirable. A proper background should be provided for chrysotherapy by treatment of infected foci and the alimentary tract thoroughly before the first injection is given. The introduction of BAL has greatly helped in the treatment of toxic complications.

Other Metals.—Other metals have been used tentatively in the hope that equal benefits might be obtained a smaller risk. Results so far indicate that bismuth and copper merit further trial.

Remission Factors.

Pregnancy.—The temporary improvement during pregnancy of the joint condition of women with rheumatoid arthritis is well known. Attempts have been made to reproduce this effect therapeutically and certain claims have been made, but further research is needed.

Histamine Antagonists.—Reports of the treatment of rheumatoid arthritis with antihistamine drugs are inconclusive, although Mutch states that in a limited experience he has obtained relief of pain with "Antistin". He considers it not unreasonable to hope that some useful application will be found for these drugs in the treatment of rheumatic disorders.

Jaundice.—In certain cases the onset of jaundice in cinchophen poisoning has been marked by a striking improvement in the condition of the joints, but attempts to copy this effect therapeutically have been unsuccessful. [The work with compound E perhaps provides an exception to this statement.]

Local Measures.

Intraarticular Injections.—Intraarticular injection therapy has been advocated for painful disorganized joints. The most popular solution used recently has been an acid solution of procaine adjusted to a pH of 5·0, but equivalent results have been obtained with a neutral solution of procaine in isotonic saline, the benefit being attributed to the psychological effect of the prompt relief afforded by the procaine and to the lubricant action of the injected fluid; even alkaline solutions appear to be helpful.

Liniments.—The use of analgesics or stimulants or combinations of the two in liniments depends on the need of the individual patient. When there is much skin hyperæsthesia a useful combination is benzyl alcohol and salicyl alcohol (saligenin) as a 5% to 10% solution in a skin-penetrating lipoid solvent such as terpineol; the stimulent effect can be reduced by replacing some of the terpineol with alcohol up to 20%, and increased by adding rubefacients such as methyl salicylate and camphor. In the absence of cutaneous tenderness, the stronger official liniments may be used. The superficial hyperæmia induced by liniments is accompanied by deep reflex vasodilatation, which it is hoped may exert a healing influence on the damaged joints.

Muscular Relaxation.

For nocturnal cramps the muscle depressant action of quinine is often useful, but the ideal drug for securing continuous relaxation of muscle spasm in active arthritis has still to be found. Several are on trial, including neostigmine, "Parpanit", "Trasentin" and "Myanesin".

Analgesics.

Salicylates, colchicum and cinchophen have specific effects in producing relief of pain. Acetylsalicylic acid is a familiar and useful analgesic. Amidopyrine has already been mentioned. Phenazone, acetanilide and phenacetin are less specific in effect than amidopyrine, but are relatively safe. For more severe pain morphine has been used, but is not satisfactory because of the development of addiction and the production of constipation. "Dilaudid" does not produce constipation, is more powerful than morphine and does not induce addiction so readily. Metopon is apparently intermediate in significant effects between morphine and "Dilaudid". Pethidine and methadon are promising in their effects, but like all the drugs of this group must be watched for their powers of producing addiction.

Various General Measures.

Production of Leucocytosis and Fever.—Drugs are sometimes used which by producing fever and leucocytosis stimulate the natural defences of the body. Leucocytosis can be sustained by drugs for short periods only. That following injection of sodium nucleinate or "Pentnucleotide" fades after a week of daily medication. Early enthusiasm for intramuscular or intravenous injection of sulphur has not been sustained.

Endocrines.—A rheumatic patient with well-defined endocrine defects is greatly benefited by their correction. Thyreoid medication is very useful for myxœdematous subjects, but is not otherwise recommended. Sex hormones have also been tried extensively, and in some cases benefit appears to have been obtained for women with osteoarthritis at and after the menopause; administration must, however, be carefully supervised and excess dosage avoided.

Vitamins.—Variations in the prothrombin content of the blood occur frequently during rheumatic fever; their relationship to salicylate medication is not simple, and there is little justification for routine administration with salicylates of vitamin *K*, which may well be reserved for definite hypothrombinæmia complicated by hæmorrhage and for the rare occasions when surgical operation is contemplated for a rheumatic patient in a hypothrombinæmic phase. Other vitamins in concentrate form may be necessary to supplement a diet restricted for therapeutic reasons. The administration of vitamin *D* in massive dosage has not produced clear benefit and is not without danger.

Correspondence.

THE PAIN OF PLEURODYNIA.

SIR: Correspondence in recent months on pleurodynia has not indicated the severity of the pain that can be encountered in this condition. A feature of an epidemic which has appeared in this district is the violent nature of the pain in about 40% of cases. The patient may roll about the bed in agony, resisting attempts at examination, during an exacerbation. This may last ten to fifteen minutes, followed by a short intermission.

Without sedation, the acute phase may last four to six hours, followed by a duller pain or "soreness". In spite of the intensity of the pain, the patient does not sweat and the pulse rate remains unaltered.

Yours, etc.,
LESLIE O'KEEFE.

Laidley,
Queensland,
September 6, 1949.

DOCTORS AND MARITAL GUIDANCE.

SIR: Doctors who are interested in problems of sex, marriage and family life are invited to a Brains Trust discussion arranged by the Sydney Marriage Guidance Council.

The Brains Trust will be composed of members of the professions chiefly involved in dealing with these problems: medical (Dr. K. S. Richardson), legal (Mr. Bryan Fuller, K.C.), religious and ethical (the Reverend Douglas Cole), social work (Miss Norma Parker), industrial welfare (Miss Ida Bye). The members of the audience will be invited to take part in the discussion. One aspect to be dealt with is the relation between the medical profession and the Sydney Marriage Guidance Centre.

The meeting is arranged for 8 p.m. on Wednesday, October 5, 1949, at Bible House, 93 Bathurst Street (between George and Kent Streets), Sydney.

Yours, etc.,
STANLEY D. MEARES.

143 Macquarie Street,
Sydney,
Undated.

THE BLIND DEAF.

SIR: As a member of the building and finance subcommittee of "The Warrawillah Home for the Blind Deaf", I would like to request, through your columns, any information concerning any persons known to be both blind and deaf. Such people have to a large extent been neglected in the past, as neither the blind nor the deaf and dumb institutions have made any special training or residential provisions for them; it is for the purpose of assisting these people that "The Warrawillah Home for the Blind Deaf" is being established.

The specific information that we require falls under two headings: (i) the number of blind deaf persons both in New South Wales and also in the whole of Australia; (ii) wherever possible the names, addresses and present circumstances of such blind deaf persons.

Yours, etc.,
ARTHUR D'OMBRAIN.

135 Macquarie Street,
Sydney,
Undated.

THE ROYAL PRINCE ALFRED HOSPITAL CANCER OF THE UTERUS FOLLOW-UP.

SIR: In reply to Dr. Alan Nelson.

Firstly, we do not regard our combined method of treatment as an alternative to radiotherapy, because our results have been consistently superior to those that have been attained by either radiotherapy or surgery alone.

Secondly, we have always cooperated with the physicist and radiotherapeutist in our work, but claim that the gynæcological clinician alone has the requisite knowledge of the female pelvis and its abnormalities and adnexal complications to say when and how radium should be placed in the genital tract.

Thirdly, we maintain our stand regarding the non-effect of radium and deep X ray on lymph nodes containing secondary squamous and adenocarcinomatous cancer deposits. We have repeatedly removed superficial inguinal lymph glands after full doses of radiotherapy by well-qualified specialists and in every case found active cancer cells still present.

We thank Dr. Nelson for his interest and assure him we will at all times cooperate with the specialists in radiotherapy in order to improve the cure rate of this fatal disease.

Yours, etc.,
HERBERT SCHLINK.

Royal Prince Alfred Hospital,
Missenden Road,
Camperdown,
New South Wales.
September 14, 1949.

CLINICAL USES OF BASAL BODY TEMPERATURE GRAPHS IN PRACTICE.

SIR: Dr. Grant's recent article in your journal on the clinical uses of basal temperature charts should be read by all general practitioners and specialists interested in sterility. The time surely is past when any woman complaining of sterility should be told, "Everything is all right, go home and keep trying"; and the temperature chart is a valuable method of keeping the patient interested during the months of investigation. It also gives her a healthy insight into the physiology of her monthly cycle.

However, in determining the optimal time for conceptional intercourse in sterility studies from the temperature chart, the beginner will have many problems to evaluate, and these have not been stressed by Dr. Grant. A very common finding is for the temperature not to rise suddenly over twenty-four hours, but to rise slowly over two, three or even four days, and physiologically this is to be expected, because the rise in temperature is due to progesterone, which is produced, following ovulation, in gradually increasing quantities by the *corpus luteum*. If ovulation takes place at the point of lowest temperature, and if the temperature takes two to four days to rise, the patient will not be aware that ovulation has occurred until at least forty-eight hours after ovulation, and according to the best authorities the ovum is only fertilizable for twenty-four hours after ovulation—thus the patient will have lost the best time for conceptional intercourse. Actually, further study of temperature charts of cycles which have resulted in conception may cause us to change our ideas on the survival period of the ovum. Professor F. J. Browne, in "Antenatal and Post Natal Care", states that "the span of life of the ovum is also relatively short and it is incapable of being fertilised for more than 24 hours after ovulation and probably less". I already have one temperature chart of a successful artificial insemination done forty-eight hours after the lowest

temperature, which, too, was associated with an intermenstrual show. The husband is a cryptorchid with aspermia, so there is no possibility of being any mistake about this conception. In this cycle one could not have definitely diagnosed ovulation by the temperature rise until seventy-two hours after ovulation—the artificial insemination was done by chance at the correct time. So that unless we can prove the ovum is fertilizable for more than twenty-four hours after ovulation, the temperature chart will be of very little use in the treatment of sterility, because I have found it exceptional for the temperature to rise two-fifths of a degree in twenty-four hours.

Finally, I do not agree with Dr. Grant that rectal temperatures are desirable or necessary. Some discriminating ex-nurse patients of mine have noticed that a minimum of ten minutes is necessary to get a maximum oral temperature reading; but in most cases oral temperatures for two to three minutes produce satisfactory biphasic charts. The taking of rectal temperatures daily for months on end is surely distasteful to many women and is likely to be given up more quickly than the taking of oral temperatures. If in an individual case a satisfactory oral chart cannot be obtained then a rectal chart can be resorted to.

Yours, etc.,

GEOFFREY HALL, M.M.S.A., D.O., R.C.O.G. (Lond.).
"Peradeniya",
262A Saint George's Terrace,
Perth.

September 9, 1949.

Obituary.

HIBBERT ALAN STEPHEN NEWTON.

BY the death of Sir Alan Newton Australian surgery has lost one of its most distinguished figures, and the cause of medical education and research a most valued champion.

Hibbert Alan Stephen Newton was born at Brighton, Victoria, on April 30, 1887, the son of Hibbert Henry Newton, Clerk of the Parliaments, Victoria, and had his early education at Haileybury College under the headmastership of Dr. Rendall, a fine scholar whose influence had a considerable effect in developing that love of literature and mastery of the English language which were so great a feature of all Newton's speeches and writings.

He graduated in 1909, which was a vintage year for Melbourne surgery; he gained the Beaney Scholarship in surgery and served as resident medical officer and later registrar at the Melbourne Hospital, proceeded M.S. in 1912 and then went to England, where he worked with Arthur Hertz (later Sir Arthur Hurst) on some of his early studies in stomach and bowel movement, and with Sir Victor Horsley at University College. He was appointed surgeon to out-patients at the Royal Melbourne Hospital in 1913, surgeon to in-patients in 1927, and on his retirement in 1946 consulting surgeon.

He commenced private practice as assistant to Mr. F. D. Bird, one of the leading surgeons of the day and one of the finest operators that Melbourne has seen. Mr. Bird went overseas at the beginning of the 1914-1918 war and Newton was left to carry on for a time, but joined the Australian Imperial Force in 1916. His work in casualty clearing stations and general hospitals was very highly commended by distinguished British and American surgeons as well as by Australians.

In 1919, before his return to Australia, Newton became a Fellow of the Royal College of Surgeons of England and he never lost his respect for the conduct of that examination which has influenced so much that of our own College. Later on he was elected an Honorary Fellow of the Association of Surgeons of Great Britain and Ireland, an Honorary Fellow of the American College of Surgeons and an Honorary Fellow of the Royal Society of Medicine. He was a Foundation Fellow of the Royal Australasian College of Surgeons, was appointed a member of Council and Honorary Secretary and Treasurer in 1929, holding office till 1933, when he was appointed Censor-in-Chief. He was President of the College from 1943 to 1945 and resigned his membership of the Council in 1947. He took a leading part in the administration of the College in drafting its Articles of Association, the building of its home in Spring Street, and all its early activities. His great capacity for quick and accurate work, his clarity of vision and prompt, wise decisions were of the utmost value in its early difficulties as well as in its later assured success. He determined from the beginning that the College would be a great and worthy thing, and set himself to make it so, and its present high standing is a great tribute to him and his fellow workers.

Always an admirer of pageantry and well-ordered ritual, he insisted that the College ceremonials should be of a high order and devoted much time and labour to perfecting them, with conspicuous success.

He was a member of the Council of the Victorian Branch of the British Medical Association and Junior Vice-President in 1937-1938, a member of the Council of the University of Melbourne, and President of the Board of the Walter and Eliza Hall Institute of Medical Research. He was knighted in 1936.

At the beginning of the second World War Newton was a prime mover in the scheme to arrange voluntary conscription of medical men for service, and this scheme was introduced more than a year before conscription for non-medical personnel was accepted. He was a member of the Central Medical Coordination Committee from 1939 to 1945 and Deputy Chairman till 1942; through the efforts of this

committee and its branches in the States the supply of medical men to the forces and the medical care of the civil population were arranged with a minimum of friction, though many men made great personal sacrifices which passed largely unnoticed by the community. From 1940 to 1942 he was consulting surgeon at Army Headquarters—a position which, though largely advisory, took up a good deal of his time.

His greatest service, however, was as chairman of the Medical Equipment Control Committee, which was formed to control the supply and use of drugs and all medical equipment. At the time of its formation the vast majority of all these stores was imported and the firms which dealt in them were in active competition with each other.

Sir Alan had to form his own team to control this work; to find out what supplies existed; how they were to be controlled and replaced, and how far manufacturers could increase their stocks; and, in many cases, to induce firms to undertake new enterprises; as well as to convince the Government of the need for all these things and to obtain its support. This he managed with the help of a very small but carefully selected staff in an amazingly successful way. Everyone—manufacturers, drug firms, importers, university scientists, the civil profession and the services—cooperated heartily, and the supplies for all were adequate, though, of course, many concessions had to be made.

That the result was so remarkably good is a high tribute not only to his great administrative ability and organizing capacity, but to his power to inspire, in all concerned, hard

work and complete confidence in his fairness and integrity. The task was a most exacting one and demanded great tact and firmness as well as colossal effort. This would have been a full-time job for most men and few could have done it at all, but he carried it through splendidly in an honorary capacity and managed to do quite a considerable, though restricted, surgical practice at the same time. The continued overwork sapped his strength, however, and in 1945 began the illness which gradually overwhelmed him. In 1947, after he had been compelled by illness to give up practice, he accepted appointment as Stewart Lecturer in Surgery in the University of Melbourne, and soon became convinced of the need to improve the facilities for teaching in the hospitals and especially to establish a better liaison between the university and the hospitals and also between the hospitals themselves.

He introduced into the hospitals as student supervisors university officers whose duty it was to aid students in their work, and to help in arrangements to cope with the overloaded curriculum. He found it necessary to oversee their work personally and made visits to one or other hospital almost daily to see how work was proceeding and to discuss any difficulties with the hospital staff. His state of health was poor and eventually he broke down completely and had to give up all this work before his schemes had been given a real test, though even then there was manifest a great advance towards lightening the student's load and helping him to obtain the best available opportunity to learn his work.

Alan Newton was a great surgeon, and his skill and sound judgement were recognized by all from very early days. He kept careful records of his cases and the patients' progress, and most of his published papers had as a basis the results of treatment of large numbers of patients followed for an adequate period. He was a harsh critic of his own work, and the mortality recorded from any procedure included every patient who died from any cause during the period of surgical treatment.

He instilled the utmost confidence into the minds of his patients and much of the striking success which he achieved in thyreoid surgery was due to the care he took in managing the patient and her attendants, and in calming her fears—though his technique was, of course, superlatively good.

As a teacher he was supreme and large numbers of practitioners, not surgeons alone, testify to the inspiration they derived from his teaching. His clinics were short and incisive, and he demanded quickness and accuracy. He was keenly interested in the progress of his students and there was always great competition for the post of his house surgeon; the fortunate holder was much envied and, provided his work was good, was helped in every way in hospital and later in practice. Newton did not suffer fools gladly and always attended to the smallest details of treatment; anything that would increase the patient's comfort had to be done at once and he had a great faculty for getting things done at once. If the fault was his he was prompt in admitting it, but he would not put up with anything second rate and had the capacity to inspire others to excel themselves.

As a lecturer or speaker on any subject he was superb; he took infinite pains in the preparation of the address and polished it for long hours till it was letter perfect, but at the time of delivery he had no notes and would speak for an hour confidently and accurately, using beautiful and cultured English. He had prodigious application and an accurate memory, and his presentation of the subject matter was as admirable as the matter itself. His name appears in the list of orators for practically every important oration sponsored by the medical profession in Australia.

Alan Newton was a man of outstanding personality and essentially a leader. He had a first-class brain and would get to the core of any problem at once, draft a detailed plan for action, and set it in train in an incredibly short time. Business experts who worked with him paid high tribute to his quick and accurate grasp of a problem and keen intelligence in solving it. He was a good churchman and a man of lofty ideals, and there is no doubt that much of his power to influence his fellow men stemmed from their certain knowledge of his honesty and integrity. Men might differ from his opinion, but no one questioned his honesty of purpose in pursuing what he believed to be right, and this he followed, relentlessly sweeping opposition aside.

He married in 1919 Mary Cicely Wicksteed and throughout his life she helped him in every way, both in his work and in dispensing most gracious hospitality to his many friends. During his long illness her untiring care and fortitude sustained him. The deepest sympathy is extended to her and to their son and daughter.

Sir Henry Newland writes: Although I had, years before, learned of Alan Newton's great gifts as a surgeon, our paths did not cross until we met in the early twenties when steps were being taken by Australian surgeons to found the Royal Australasian College of Surgeons.

I was at once impressed by Newton's personality, physical and intellectual. He was a clear thinker, quick to grasp essentials and terse in his exposition of them. There was no beating about the bush. He threw himself heart and soul into the task, no easy one, of moulding the constitution of the College on lofty lines. In due course he became Censor-in-Chief, and no one could fail to be struck by the efficiency and dignity with which the affairs and scientific functions of the College were organized and conducted.

His fine presence, his crisp, cultured, concise utterance conveyed a sense of a dominating personality to those who heard him speak, whether in private, from a dais, or in the Royal Melbourne Hospital, which he loved so well.

My official association with him during the six years (1929-1935) when I was President of the College, and later on, during the life of the Central Medical Coordination Committee, grew into a very cordial and lasting friendship.

It is much to be regretted that Alan Newton's burning energies should have been quenched at a time when there is still so much for him to do, and the nation's need of men like him is so great.

Dr. Victor Hurley writes: The death of Sir Alan Newton has removed one of the outstanding figures of Australian surgery.

From the time he entered the Medical School of the University of Melbourne in 1905, teachers and fellow students alike recognized that with his personality, energy and ability, he was destined to become one of the leaders of his chosen profession.

During the thirty years or more he was on the staff of the hospital, he set a consistently high standard in all his work, and required the same from all those who worked under him. His residents, students and nurses, appreciating that his objectives were efficiency and the welfare of the patients, always rendered loyal and devoted service. He was ready and generous to appreciate and encourage good work, but slackness or inefficiency would bring merited reproof in terms often sharp, incisive, and sometimes devastating.

He was a Foundation Fellow of the Royal Australasian College of Surgeons, and almost from its inception took an active part in its affairs. In the earlier years of the College he was a tower of strength, and as its development proceeded, he undertook more and more of the work involved in shaping its policy and administering its affairs. He and Sir Hugh Devine were largely responsible for the successful negotiations which secured for the College its present site, and also for the building which now houses its activities. He successively occupied the positions of Member of Council, Censor-in-Chief, Vice-President and President of the College, and its progress during the twenty-three years since its foundation is largely due to his foresight and sound judgement.

In the second World War, as chairman of the Medical Equipment Control Committee, he undertook the difficult and highly complex task of ensuring that medical supplies and equipment would be available for the needs of the services as well as of the civil community. We were dependent before the war on overseas sources for many essentials. The organization had to be created *de novo*—new sources of supply arranged—and local manufacture and production undertaken for many things which had not previously been produced in Australia. His forceful and unconventional methods, particularly in dealing with government departments, were most effective. By short cuts and avoidance of red tape, he obtained results which would have been quite unattainable by ordinary departmental methods operating through the usual official channels. The success of the work of this committee for which he was almost entirely responsible was one of the outstanding achievements of the war.

Even at this time his health was not good, as he never seemed to have recovered completely from a severe pneumonia he had shortly before the war. He continued, however, to throw himself with characteristic energy into the various activities with which he was associated, and actually undertook additional responsibilities.

After the war he retired from the active staff of the hospital at the termination of his period of appointment, and was elected to the council of the university. This gave him opportunity to develop plans for the university to undertake a greater degree of responsibility for clinical teaching in the hospitals, and a closer integration between

the university and the clinical schools. He was appointed Director of Clinical Studies in order to carry out these plans.

He also was appointed chairman of the Board of the Walter and Eliza Hall Institute of Medical Research and took an active part in its affairs.

His work on these and other bodies was interrupted from time to time in the last two or three years by further breakdowns in his health. Nevertheless, he continued to maintain his interest in them, and worked energetically, though often under considerable physical difficulties, almost up to the last.

His qualities were well appreciated outside the profession, and he counted among his close friends many of the leaders of the community in other walks of life. His keen intellect, strong personality and capacity of lucid exposition would have ensured an equally distinguished career at the bar. Actually he came of a family which has supplied in the past several leading members of the legal profession.

He was an excellent public speaker, was widely read, and was possessed of a remarkable memory. He always carefully prepared his subject, and after writing and rewriting his speech until he was satisfied, would then deliver it almost word for word as it had been written without reference to any notes.

His fame and reputation will long be remembered. His full worth will be judged not only by what he accomplished in his own lifetime, but also by his continuing influence which will be felt on the work and thought of those following after him.

The sympathy of a large circle of friends is extended to his widow, a son now practising at the bar in Melbourne, and a daughter on the teaching staff of the University of Melbourne.

IVAN BLAUBAUM.

WE regret to announce the death of Dr. Ivan Blaubaum, which occurred on September 15, 1949, at Melbourne.

ROBERT SPENCER GODSALL.

WE regret to announce the death of Dr. Robert Spencer Godsall, which occurred on September 19, 1949, at Bellevue Hill, New South Wales.

Australasian Medical Publishing Company, Limited.

ANNUAL MEETING.

THE annual meeting of the Australasian Medical Publishing Company, Limited, was held at The Printing House, Seamer Street, Glebe, New South Wales, on September 14, 1949, Sir Henry Newland in the chair.

Directors' Report.

The report of the directors of the company was as follows:

The directors submit their report for the twelve months ended June 30, 1949, together with the balance sheet as at June 30, 1949, and the profit and loss account for the twelve months ended June 30, 1949.

It is with regret that we report the death in Melbourne on April 6, 1949, of Dr. Crawford Henry Mollison, who was an original member of the company. Dr. Robert Southby has been nominated by the Victorian Branch of the British Medical Association to fill the vacancy in the membership.

The number of pages of reading matter in THE MEDICAL JOURNAL OF AUSTRALIA was increased during the year and the journal maintains its high standard.

The result of the year's production in the printing and publishing department was satisfactory and a small surplus remains after providing for depreciation and taxation.

The company's reserves are used in the business and we consider the state of the company's affairs is satisfactory.

DISEASES NOTIFIED IN EACH STATE AND TERRITORY OF AUSTRALIA FOR THE WEEK ENDED SEPTEMBER 10, 1949.[1]

Disease.	New South Wales.	Victoria.	Queensland.	South Australia.	Western Australia.	Tasmania.	Northern Territory.[2]	Australian Capital Territory.	Australia.[3]
Ankylostomiasis	*	..	..	..	*	..	..	..	..
Anthrax	*	..	..	..	..	..	..	..	..
Beriberi	*	*	*	*	*	*	..	*	..
Bilharziasis	*	..	..	..	..	..	..	..	..
Cerebro-spinal Meningitis	4(3)	2(1)	..	..	1(1)	..	..	..	7
Cholera	..	..	..	..	..	..	..	..	..
Coastal Fever(*a*)	*	*	..	*	*	*	*	*	..
Dengue	*	*	*	*	*	*	..	*	..
Diarrhœa (Infantile)	..	..	3(3)	..	..	..	..	..	3
Diphtheria	11(5)	6(2)	3	..	3(2)	..	..	..	23
Dysentery(*b*)	*	..	4(4)	..	..	..	..	..	4
Encephalitis Lethargica	..	..	..	..	..	..	..	..	..
Erysipelas	*	*	*	..	*	*	..	..	..
Filariasis	*	..	..	..	..	..	..	..	..
Helminthiasis	*	..	*	*	*	*	*	*	..
Hydatid	*	1	*	*	..	*	*	..	1
Influenza	*	*	*	..	*	*	..	*	..
Leprosy	..	..	..	..	1	..	..	..	1
Malaria(*c*)	*	(*c*)	(*c*)	(*c*)	(*c*)	1(1)(*c*)	(*c*)	(*c*)	1(*c*)
Measles	*	*	*	91(18)	*	*	..	..	91
Plague	..	..	..	..	..	..	..	..	..
Poliomyelitis	6(3)	52(28)	..	19(16)	2(2)	1(1)	..	1	80
Psittacosis	*	..	*	..	*	*	*	*	..
Puerperal Fever	..	..	..	..	..	..	..	..	..
Rubella	*	*	*	*	*	*	..	..	..
Scarlet Fever	26(16)	37(13)	15(5)	8(6)	2(1)	1	..	..	89
Smallpox	..	..	..	..	..	..	..	..	..
Tetanus	*	..	*	*	1(1)	*	*	*	1
Trachoma	*	..	*	*	*	*	*	*	..
Tuberculosis(*d*)	30(10)	21(10)	6(4)	4(4)	6(4)	8(3)	..	1	76
Typhoid Fever(*e*)	..	..	..	..	..	..	..	..	..
Typhus (Endemic)(*f*)	..	..	1	..	..	..	..	..	1
Undulant Fever	*	*	..	*	1(1)	*	*	*	1
Weil's Disease(*g*)	*	*	*	*	*	*	*	*	..
Whooping Cough	*	*	*	14(5)	*	*	..	..	14
Yellow Fever	..	..	..	..	..	..	..	..	..

[1] The form of this table is taken from the *Official Year Book of the Commonwealth of Australia*, Number 36, 1944-1945. Figures in parentheses are those for the metropolitan area.
[2] Figures not available.
[3] Figures incomplete owing to absence of returns from Northern Territory.
* Not notifiable.
(*a*) Includes "Mossman" and "Sarina" fevers. (*b*) Includes amœbic and bacillary. (*c*) Statistics inexact with varying practice with regard to relapses in Service cases infected overseas. (*d*) Includes all forms except in New South Wales and Northern Territory, where only pulmonary tuberculosis is notifiable. (*e*) Includes enteric fever, paratyphoid fevers and other Salmonella infections. (*f*) Cases reported include scrub, murine and tick typhus. (*g*) Includes leptospiroses, Weil's and para-Weil's disease.

Provision has been made for the payment of debenture interest for the year ended June 30, 1949.

Sir Henry S. Newland and Dr. W. F. Simmons retire from office by rotation in accordance with the Articles of Association (Article 39). They are eligible and present themselves for reelection.

H. S. NEWLAND,
September 14, 1949. Chairman.

Election of Directors.

Sir Henry Newland and Dr. W. F. Simmons were reelected to the Board of Directors.

Australian Medical Board Proceedings.

NEW SOUTH WALES.

THE undermentioned have been registered, pursuant to the provisions of the *Medical Practitioners Act*, 1938-1939, of New South Wales, as duly qualified medical practitioners:

Hobart, William Robert, M.B., B.S., 1946 (Univ. Queensland), District Hospital, Manly.

Riddell, Rees James, M.B., B.S., 1935 (Univ. Melbourne), D.T.M. and H. (London), 1939, Commonwealth Health Laboratory, Albury.

Slade, John Harman, M.B., B.S., 1946 (Univ. Adelaide), Saint Vincent's Hospital, Darlinghurst.

Thatcher, Ralph Arnold, M.R.C.S. (England), L.R.C.P. (London), 1935, M.R.C.O.G., 1948, 303 Blackwall Road, Woy Woy.

The following additional qualifications have been registered:

Hogan, Allan Barry, 139 Macquarie Street, Sydney (M.B., B.S., 1941, Univ. Sydney), M.R.A.C.P., 1948.

Hooper, Francis Maxwell, 173 Bay Street, Brighton-le-Sands (M.B., B.S., 1945, Univ. Sydney), D.D.R., 1949, Univ. Sydney.

Leventhal, Frank, Ithaca Road, Elizabeth Bay (M.B., B.S., 1944, Univ. Sydney), Dip. Anæs., 1949, Univ. Sydney.

McGuinness, Alan Edward, 139 Macquarie Street, Sydney (M.B., B.S., 1935, Univ. Sydney), M.R.C.P., London, 1940, M.R.A.C.P., 1948.

Shirley, Anthony David, Cootamundra (M.B., B.S., 1941, Univ. Sydney), D.C.H. (R.C.P. and S.), 1948.

Nominations and Elections.

THE undermentioned has applied for election as a member of the New South Wales Branch of the British Medical Association:

Anderson, Douglas Rea, M.B., B.S., 1947 (Univ. Sydney), 11 Everton Road, Strathfield.

The undermentioned have been elected as members of the New South Wales Branch of the British Medical Association:

Collings, Bruce, M.B., B.S., 1948 (Univ. Sydney), Sydney Hospital, Sydney.

Dunkley, Brian Hiatt, M.B., B.S., 1947 (Univ. Sydney), Ryde District Soldiers' Memorial Hospital, Eastwood.

Freedman, Albert, M.B., B.S., 1947 (Univ. Sydney), Saint Vincent's Hospital, Darlinghurst.

Pearce, Raymond William, M.B., B.S., 1948 (Univ. Sydney), 23 Darling Point Road, Darling Point.

Taylor, Robert Gregory Darnley, M.B., B.S., 1945 (Univ. Sydney), Whitehall, 28 Great North Road, Five Dock.

Farb, Max, M.B., Ch.B., 1945 (Univ. New Zealand), 12 Ormonde Parade, Hurstville.

Notice.

A REQUEST has been received from Holland for the following numbers of THE MEDICAL JOURNAL OF AUSTRALIA: Volume II, 1940, Numbers 15 and 16; Volume I, 1941, Number 21; Volume II, 1941, Numbers 1, 5, 7, 8, 9, 12, 18 and 25. The Australasian Medical Publishing Company, Limited, is prepared to buy these journals from any reader who can make them available.

Medical Appointments.

Dr. C. J. Helman has been appointed honorary assistant anæsthetist at the Royal Adelaide Hospital, Adelaide.

Diary for the Month.

OCT. 4.—New South Wales Branch, B.M.A.: Council Quarterly.
OCT. 5.—Victorian Branch, B.M.A.: Branch Meeting.
OCT. 5.—Western Australian Branch, B.M.A.: Council Meeting.
OCT. 6.—South Australian Branch, B.M.A.: Council Meeting.
OCT. 7.—Queensland Branch, B.M.A.: Branch Meeting.
OCT. 11.—New South Wales Branch, B.M.A.: Executive and Finance Committee.
OCT. 11.—New South Wales Branch, B.M.A.: Organization and Science Committee.
OCT. 13.—Victorian Branch, B.M.A.: Organization Subcommittee.
OCT. 14.—Queensland Branch, B.M.A.: Council Meeting.
OCT. 17.—Victorian Branch, B.M.A.: Finance, House and Library Subcommittee.
OCT. 18.—New South Wales Branch, B.M.A.: Medical Politics Committee.

Medical Appointments: Important Notice.

MEDICAL PRACTITIONERS are requested not to apply for any appointment mentioned below without having first communicated with the Honorary Secretary of the Branch concerned, or with the Medical Secretary of the British Medical Association, Tavistock Square, London, W.C.1.

New South Wales Branch (Honorary Secretary, 135 Macquarie Street, Sydney): Ashfield and District United Friendly Societies' Dispensary; Balmain United Friendly Societies' Dispensary; Leichhardt and Petersham United Friendly Societies' Dispensary; Manchester Unity Medical and Dispensing Institute, Oxford Street, Sydney; North Sydney Friendly Societies' Dispensary Limited; People's Prudential Assurance Company Limited; Phœnix Mutual Provident Society.

Victorian Branch (Honorary Secretary, Medical Society Hall, East Melbourne): Associated Medical Services Limited; all Institutes or Medical Dispensaries; Australian Prudential Association, Proprietary, Limited; Federated Mutual Medical Benefit Society; Mutual National Provident Club; National Provident Association; Hospital or other appointments outside Victoria.

Queensland Branch (Honorary Secretary, B.M.A. House, 225 Wickham Terrace, Brisbane, B.17): Brisbane Associated Friendly Societies' Medical Institute; Bundaberg Medical Institute. Members accepting LODGE appointments and those desiring to accept appointments to any COUNTRY HOSPITAL or position outside Australia are advised, in their own interests, to submit a copy of their Agreement to the Council before signing.

South Australian Branch (Honorary Secretary, 178 North Terrace, Adelaide): All Lodge appointments in South Australia; all Contract Practice appointments in South Australia.

Western Australian Branch (Honorary Secretary, 205 Saint George's Terrace, Perth): Wiluna Hospital; all Contract Practice appointments in Western Australia. All government appointments with the exception of those of the Department of Public Health.

Editorial Notices.

MANUSCRIPTS forwarded to the office of this journal cannot under any circumstances be returned. Original articles forwarded for publication are understood to be offered to THE MEDICAL JOURNAL OF AUSTRALIA alone, unless the contrary be stated.

All communications should be addressed to the Editor, THE MEDICAL JOURNAL OF AUSTRALIA, The Printing House, Seamer Street, Glebe, New South Wales (Telephones: MW 2651-2.)

Members and subscribers are requested to notify the Manager, THE MEDICAL JOURNAL OF AUSTRALIA, Seamer Street, Glebe, New South Wales, without delay, of any irregularity in the delivery of this journal. The management cannot accept any responsibility or recognize any claim arising out of non-receipt of journals unless such notification is received within one month.

SUBSCRIPTION RATES.—Medical students and others not receiving THE MEDICAL JOURNAL OF AUSTRALIA in virtue of membership of the Branches of the British Medical Association in the Commonwealth can become subscribers to the journal by applying to the Manager or through the usual agents and booksellers. Subscriptions can commence at the beginning of any quarter and are renewable on December 31. The rate is £3 *per annum* within Australia and the British Commonwealth of Nations, and £4 10s. *per annum* within America and foreign countries, payable in advance.